THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—38TH YEAR. SYDNEY, SATURDAY, JANUARY 20, 1951. No. 3.

Table of Contents.

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ORIGINAL ARTICLES— Page.

The Lewis (Le[a]) Blood Group and Secretor Types. A Review: Their Correlation in the Blood and Saliva of White Australians, by R. T. Simmons, N. M. Semple and J. J. Graydon 105
Ætiology of Diabetes Mellitus, by Ewen Downie 110
Pathological Aspects of Diabetes, by W. E. King 113
Why Diet the Diabetic?, by Bruce Hunt, M.D., M.R.C.P., F.R.A.C.P. 114
Diabetic Prevalence in New South Wales, by H. O. Lancaster 117
An Anti-Insulin Factor in the Plasma of Diabetic Patients, by J. Bornstein and Phyllis Trewhella 119

REVIEWS—

Further Rare Diseases 123
Malariology 123
Radiotherapeutic Practice 124
The Hinge Graft or Ginglymus Implant 124
Biochemistry 124

LEADING ARTICLES—

The Hospital Almoner Problem 125

CURRENT COMMENT—

Measures to Lessen the Hazards of Boxing 126
Homologous Serum Hepatitis 126
Intractable Peptic Ulcer 127

ABSTRACTS FROM MEDICAL LITERATURE—

Pathology 128
Morphology 129

BRITISH MEDICAL ASSOCIATION NEWS—

Scientific 130

CORRESPONDENCE— Page.

Gestational Rubella and Therapeutic Abortion .. 132
Australian Red Cross Appeal for Drug Samples .. 133
Care and Management of Laboratory Animals .. 133
Congenital Deaf-Mutism, Pigmentary Degeneration of the Retina, and Amentia 133
Treatment of Eczema 133
Ocular Manifestations of Sarcoidosis with a Description of Seven Cases 134
Post-Graduate Hospital Posts in England 134
Occupational Ophthalmology 134

OBITUARY—

Thomas Rhodes Matson 134
Rupert Gordon Weaver 135
Clive Nelson Pitt 135
George Wade Sinclair 135
George Edward Murphy 135

MEDICAL PRACTICE—

Police Offences (Amendment) Act, 1908, as Amended 135

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA 135

MEDICAL APPOINTMENTS 136

NOMINATIONS AND ELECTIONS 136

DIARY FOR THE MONTH 136

MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. 136

EDITORIAL NOTICES 136

THE LEWIS (Le[a]) BLOOD GROUP AND SECRETOR TYPES. A REVIEW: THEIR CORRELATION IN THE BLOOD AND SALIVA OF WHITE AUSTRALIANS.

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THE purpose of this paper is to review the current literature on the Lewis blood group and its correlation with the secretion of A, B or H substances in body fluids, and to present Lewis blood group and secretor findings in white Australians.

THE LEWIS BLOOD GROUP.

The discovery of a "new" blood group designated Lewis was reported by Mourant (1946). The Lewis antigen was found to be present in about 25% of 96 English blood samples tested, and was shown to be independent of the A B O, M–N, Rh, P, Lutheran and Kell systems.

Prior to Mourant's announcement a new antigen and antibody were being investigated in Melbourne, but these were subsequently shown to be identical with those described by Mourant (Jakobowicz, Simmons and Bryce, 1947). This investigation was complicated by the presence in the serum containing the new agglutinin of a second antibody, which proved to be anti-hr′ (anti-c). Krieger and Simmons (1949) described a further Australian example of anti-Lewis. Both of these Lewis anti-sera were detected following evidence of blood transfusion reactions.

Andresen (1947) reported that he and Friesleben, working independently in Copenhagen, had found an agglutinin in the serum of eight mothers which, when tested with blood samples from adults, agglutinated 21%. He showed that these reactions were determined by a new blood group system which, as it was unrelated to previously described blood factors, was designated the L system, and the phenotypes demonstrated were termed "L+" and "L–". He found that L+ reactions in young children varied according to age: in children to the age of three months 79% gave L+ reactions, from four to six months 73% gave L+ reactions, from seven to nine months 36% gave L+ reactions, and in a group of ten to twelve months the L+ percentage fell to 29.

Andresen further showed that L– parents might have L+ children. He suggested that two genes, L and l, were involved, L representing the character demonstrated, and l its absence. In adults, the LL homozygotes gave the L+ reaction, while in young children, the heterozygotes Ll as well as LL, gave the L+ reaction. In adults Ll and ll persons were non-reactors—that is, L—and this was explained on the grounds that l in adults was a dominant character. It was suggested that l progressively became dominant over L during the first twelve months of life.

The L system of Andresen was subsequently proved to be identical with the Lewis system established by Mourant in 1946.

Andresen (1948) reported the discovery of a related agglutinin which he called anti-L_2. In this report he referred to his original anti-L, shown to be identical with anti-Lewis, as anti-L_1.

In a series of 238 group O blood samples tested with both anti-L_1 and anti-L_2 sera, it was found that 20% were anti-L_1 positive, but were not agglutinated by anti-

L_2, a further 74% not agglutinated by anti-L_1 were agglutinated by anti-L_2, and 6% of the samples failed to agglutinate with either serum. Thus an almost completely antithetical relationship in reactions was shown between the two sera. He found that the receptor L_2 is much more frequent in adults than in children, which is the converse of the finding with the L_1 receptor. While group O and group A_2 cells both gave over 70% of positive reactions with anti-L_2, it was found that the percentage of positive reactions with group A_1 cells was only 42. Andresen suggested that this unexpected finding could be explained on the grounds that the presence of the A_1 receptor in red cells inhibits the development of the L_2 receptor, such an effect in genetics being designated epitasy. However, the epitasy in this instance was incomplete, as not all A_1 cells failed to agglutinate. Some A_1 cells gave weak reactions and with others the reactions were uncertain.

In the tests with group O cells referred to above, it was seen that 6% of the cells tested gave negative results with both anti-L_1 and anti-L_2 sera. Thus, at this stage, Andresen pointed out that it was not possible to establish the genetics of inheritance with certainty.

Grubb (1948) reported his observation on the correlation of the Lewis blood group reactions and the secretor character in man. He noticed that of 20 Lewis-positive individuals all were non-secretors of the A, B or H blood group-specific substances, while of 42 Lewis-negative persons, 41 were secretors, and one, the only exception, was a non-secretor.

This observation was of great importance, because a positive or negative Lewis blood group response was shown to be directly related to an individual's ability to secrete blood group-specific substance in the saliva or body fluids. As a result, a new field of study became available with fresh problems in human genetics to be solved.

The use of the term H substances instead of the so-called O substance in human secretions originates from the observations of Morgan and Watkins (1948), who classified sera agglutinating cells of group O into two types, anti-H and anti-O.

They defined the group of H antibodies as those consisting of the hetero-antibodies Shigella goat-immune and cattle anti-O reagents, and an unknown proportion of human anti-O reagents. The H antibodies are strongly active on human blood cells of groups O, A_2 and A_2B, and give weaker and unreliable reactions with cells of groups B, A_1 and A_1B. Anti-H sera are easily inhibited by human saliva independently of the A B O genotype of the individual.

The group of O antibodies of human origin agglutinates a product of the O gene in human red cells. These antibodies are not inhibited in their activity by human saliva.

Nomenclature.

At a meeting in England of the Committee on Nomenclature and Notation in Human Genetics which was made possible by the World Health Organization, a notation for the Lewis and Lutheran blood group systems was adopted (Andresen, Callender *et alii*, 1949). The nomenclature for the genes, genotypes, phenotypes and antibodies as accepted for each system is set out in Table I.

Also at that meeting the duplication of the S–s notation relative to the salivary secretion of A, B or H substances on one hand, and to the recently discovered subgroups of the M–N system, was considered. It was decided that since this duplication had not so far caused confusion, no recommendation of changes in the use of S and s should be made pending further work on the Le system.

To hold a decision of this nature in abeyance may be wise; but we consider that a change is desirable and should be made as soon as possible. While members of the committee at the above-mentioned meeting stated that they had not encountered an instance of confusion in the use of this duplicated terminology, such has not been our experience.

Andresen and Jordal (1949) described an incomplete (blocking) antibody related to the Lewis system, which was found in the serum of an A_1 Le (a–b–) mother. It

TABLE I.

Notation for the Lewis and Lutheran Systems Adopted by the English Committee on Nomenclature and Notation in Human Genetics.

	Lewis System.	Lutheran System.
Genes	Le^a Le^b	Lu^a Lu^b
Genotypes	Le^aLe^a Le^aLe^b Le^bLe	Lu^aLu^a Lu^aLu^b Lu^bLu^b
Phenotypes ..	Le(a+ b−) Le(a− b+) Le(a− b−)	Lu(a+) Lu(a−)
Antibodies	anti-Le^a anti-Le^b	anti-Lu^a

was shown that the serum contained an anti-Le^a agglutinin and an incomplete antibody which reacted with about 90% of all blood samples, when the test cells were suspended in their own plasma or in albumin. (Jakobowicz, Simmons and Bryce, 1947, had also found in a specimen of serum an incomplete antibody associated with anti-Lewis which, when tested at 37° C. with cells suspended in albumin, gave approximately 90% of positive reactions. As the result of several hundred tests with cells of known blood types, it was shown that the non-reactors all lacked the hr′(c) antigen. Further, a pronounced double-dose effect with the c antigen was noticed. It was proved conclusively in their case that the incomplete antibody they investigated was anti-c.) Andresen and Jordal tested their serum, called anti-X, with some 300 blood samples. All anti-X negative cells were found to be Le (a–b–), and in the case of groups O and A_2, all Le (a–b–) cells were also anti-X negative. These workers found that anti-X reacted only at room temperature, whereas their anti-Le^a reacted at 37° C. Anti-X serum differed from anti-Le^b in that it gave (i) the same percentage of reactors in groups O and A_1, and (ii) approximately the same percentage of reactors in adults and children. Absorption with Le (a+b–) cells removed all agglutinins from both anti-Le^a and anti-X sera. Andresen and Jordal suggested that X is an inherited factor, that a corresponding allele x must also exist, and further, that the homozygote XX inhibits the development of phenotypes of the Lewis system.

Brendemoen (1949), working in Norway, reported the discovery of two further examples of anti-Lewis serum.

Among 285 individuals of group A_1, A_2 and O, 21·75% were found to be Lewis-positive. The serum and saliva of 49 persons were examined for the presence of Lewis group-specific substances. Only Lewis-positive persons showed the presence of Lewis group-specific substances in their serum, while it was possible to demonstrate Lewis group-specific substances in 41 (83·7%) of 49 saliva samples. The substances were found to be demonstrable in saliva from both Lewis-positive and Lewis-negative persons, but not in all samples tested.

Race, Sanger, Lawler and Bertinshaw (1949) tested with anti-Le^a serum the blood of 571 individuals, consisting of 406 English, 33 Welsh and 132 American whites, and found that 130 (22·7%) were Le (a+). They reported in detail their findings on the Lewis blood groups of 79 families, and an analysis made of these results strongly supported the contention of Andresen that adults whose red cells are Le (a+), are genetically homozygous—that is, Le^aLe^a. It was stated that more than half of the 79 families were also tested with anti-Le^b serum, and of the blood samples tested those

belonging to group O, A_2, B or A_2B were, with four exceptions, agglutinated either by anti-Le^a or by anti-Le^b, but never by both. The four exceptions, from unrelated persons, gave unequivocally negative results with both anti-sera. No other details of their findings with anti-Le^b serum were given, but it was said that more families were being tested in the hope of throwing further light on the genes involved in the Lewis blood groups.

Saliva samples from 172 members of the above families (parents and children) were tested for the presence of A, B or H substances. The results obtained, when considered in relation to the Lewis (Le^a) blood groups, confirmed the observation of Grubb that there is a close, if not absolute, association between Le (a+) red cells and non-secretory saliva, and that the converse relationship is close, though not absolute.

Grubb and Morgan (1949) tested the red cells of 212 unrelated English individuals and showed that 47 (22·2%) were Le (a+). Saliva samples from the same 212 individuals were tested for the presence of A, B or H substances, and 49 (23·1%) were non-secretors of these substances.

It was shown that Le^a and Le^b substances were present in secretions (saliva and ovarian cyst fluid) of individuals of the appropriate genotype, and that these substances showed the same general and physical characters as the A, B and H substances. Le^a substance was also shown to be present in gastric juice and serum. Thus, serum at a dilution of 1:2 from a person of genotype Le^aLe^a neutralized a strongly agglutinating dose of anti-Le^a serum, whereas serum from a person of phenotype Le (a–b–) was without inhibitive power. Some ovarian cyst fluids were proved to be a convenient and potent source of Le^a and Le^b substances.

Saliva samples at a dilution of 1:5 from 30 Le (a+) persons all neutralized Le^a serum, while 42 (84%) of 50 saliva samples from Le (a–) persons also neutralized Le^a serum when the saliva samples were used at the same dilution. It was thought probable that all persons possessing the Le^a gene secrete Le^a substance. It was pointed out, however, that differentiation of secretors from non-secretors in the ABO system is not without difficulty in some instances. The results of the above studies indicated that the Le^a secretion–non-secretion phenomenon represents a more gradual and continuous variation than is met with in A–B–H secretion–non-secretion.

It was suggested that the Lewis genes Le^a and Le^b, the secretor gene S and non-secretor gene s belong to one and the same system. This work performed in England confirms and considerably extends the independent observations of Brendemoen published two months earlier.

Dunsford (personal communication), working at the Blood Transfusion Laboratory, Sheffield, England, where some 60,000 to 70,000 antenatal cases are investigated yearly, has found over 30 examples of anti-Le^a serum and two of anti-Le^b.

Simmons and Graydon (1950) reported preliminary findings of the data set out in the present paper. At the time of their report 29·2% Le (a+) blood samples were found in 500 of group O tested. In tests of 164 corresponding blood and saliva samples collected from individuals of groups O, A, B and AB, there was correlation between Lewis and secretor reactions in 163. The one exception found was an individual of subgroup A_1 who, on repeated tests, was shown to be Le (a–) and a non-secretor. A simple slide technique for performing Le^a tests was given. It was considered that the excellent correlation obtained between the Le^a and secretor reactions indicated the correctness of the Le^a and secretor readings. Preliminary data on the Le^a reactions obtained with blood samples from various races were reported. Good correlation had been obtained in the results of Lewis and secretion tests in Australian aborigines.

THE SECRETOR AND NON-SECRETOR TYPES: S–s SYSTEM.

The relevant literature concerning the discovery and investigation of group-specific substances in saliva and body fluids has been summarized by Wiener (1943).

Lehrs (1930) and Putkonen (1930) were the first to establish the fact that the saliva of certain individuals of groups A, B and AB contains the corresponding group-specific substances in higher concentration than in the red blood cells. On the other hand, such substances were shown to be absent in the saliva of other individuals of the same blood groups.

Schiff and Sasaki (1932) designated the former type "secretors" and the latter type "non-secretors". They showed that group O individuals could also be subdivided in a similar manner by testing their saliva with anti-O sera. They demonstrated the hereditary nature of the characters secretor and non-secretor in a series of 50 families with 149 children. It was shown that the ability to secrete group-specific substances was transmitted as a simple Mendelian dominant. No evidence of linkage was found between the secretor character and the A, B, M and N agglutinogens.

It was later shown that group-specific substances could be isolated in two forms, (*a*) water-soluble and (*b*) alcohol-soluble. The ability or inability to secrete group-specific substances is a constant trait of the individual. When these substances are absent from the saliva they are also absent from other secretions, such as urine, tears, semen, gastric juice and milk.

Wiener and Belkin (1943) obtained results which disagreed with those of Hartmann (1941), relative to the presence of group-specific substances in the newborn. They tested 30 pairs of saliva samples from mothers and new-born infants, and found that the distinction between secretors and non-secretors was as sharp in infants as in the mothers, which indicated that this character was fully developed at birth.

The secretor character S and the non-secretor character s have some application in forensic medicine.

MATERIALS AND METHODS.

The 1123 blood samples tested in this investigation were collected from members of the staff of these laboratories and from blood donors. The samples consisted of four large drops of blood added to one millilitre of glucose-citrate blood-preserving fluid (Simmons and Graydon, 1945), to give cell suspensions of about 8% to 10%.

The anti-Le^a serum (Mrs. M.P.) of group O used throughout this investigation was that described by Jakobowicz *et alii* (1947). After storage for over four years at 5° C., there was no appreciable loss in its activity. The serum reacted both at room temperature (20° C.) and at 37° C., but much stronger reactions were obtained at room temperature. Its reactions had been compared with four samples of anti-Lewis given to one of us by Dr. A. Mourant, and with another found locally, and it gave the strongest reactions of all six sera (Krieger and Simmons, 1949). Unpublished observations made in 1946 on Mrs. M.P.'s serum show that all attempts to neutralize the anti-A and anti-B agglutinins present by the addition of saliva completely inactivated its Lewis activity. Similar results were obtained when Dr. Rachel Jakobowicz added dried saliva from group A and group B individuals. The effect was considered to be unusual, but was not further investigated at the time. More recently, the anti-A and anti-B agglutinins have been neutralized by the addition of dried A and B substances prepared by us from animal sources. The 500 group O blood samples collected for this survey were tested with the untreated group O serum, while the remaining 623 samples of groups A_1, A_2, B and AB were tested with the neutralized serum. Samples of this serum in the wet state have been sent to America and excellent reactions with it have been reported to us.

The Le^a Blood Tests.

The tests were carried out on glass slides by the following simple technique: to one drop of the undiluted serum was added one drop of an 8% to 10% cell suspension and the slide rotated to ensure thorough mixing of the cells and serum. The slides were then placed in a moist chamber at room temperature (20° C.) for fifteen minutes, after which they were removed and tilted back and forth very gently once or twice. Spectacular and complete agglutination was consistently obtained with Le(a+) cells, which

presumably were of the homozygous genotype Le^aLe^a. A certain percentage of weak reactions appearing after fifteen minutes has been noted in all blood groups, and these may represent reactions with some heterozygous Le^aLe^b cells. Originally it was thought that these weak reactions were due to an extra cold agglutinin, because most of them were not evident at 37° C. Perhaps the most important detail to be noted in this technique is the use of approximately 10% cell suspensions made by adding the blood directly to the glucose-citrate solution.

It may be stated that all tests in this laboratory for groups, subgroups, M N S types, Rh types, C^w, D^u, P *et cetera*, are performed on clear glass slides with selected sera, *versus* 8% to 10% unwashed cell suspensions, at either room temperature or 37° C. as the case requires.

During the course of this work it has been possible to study the reliability of Le^a reactions obtained with blood samples stored in the glucose-citrate blood-preserving fluid at 5° C. for periods up to six months. It has been shown that completely reliable results with anti-Le^a serum were obtained during this period. The only modification of the technique for testing old cell samples has been to extend the time of reading the tests from fifteen to sixty minutes at 20° C. The experience gained in Lewis and secretor tests has enabled us successfully to add these genetic tests on blood and saliva samples to those already being performed as a routine. The results of Lewis and secretor tests on samples from native races in Australia, Borneo, New Zealand and the Marshall Islands have shown fair correlation. The reports of findings on these and other native races will be published at a later date.

Determination of A, B or H Secretion in Saliva.

The tests for A, B or H secretion in saliva were performed by the inhibition of agglutination method as follows.

Collection of Saliva Samples.

All saliva samples were collected in sterile six inch by one inch test tubes and were placed in boiling water for thirty minutes, within fifteen minutes of collection. Only in odd cases was subsequent centrifugation necessary.

Tests for Secretion of A and B Group-Specific Substances.

The tests for A and B group-specific substances were carried out on saliva from individuals of groups A, B and AB. The anti-A and anti-B sera used were pooled high-titred human sera especially selected for blood grouping. Each serum had a titre of 1:320 and gave complete agglutination at a dilution of 1:40 in saline.

Four drops of anti-A or anti-B serum diluted 1:10 in saline and an equal volume of saliva diluted 1:10 in saline were well mixed in small tubes (seven millimetres internal diameter). The mixture was allowed to stand for thirty minutes at room temperature (20° C.). Four drops of a 1% saline suspension of group A_1 or group B once-washed cells were then added. The mixtures were allowed to stand at room temperature for one hour, and then were examined for the presence or absence of agglutination.

Tests for Secretion of H Substance in the Saliva of Group O Individuals.

The anti-H serum used in the tests was a sample generously given to one of us in 1947 by Dr. W. T. J. Morgan. Samples of four human anti-O sera available to us were not neutralized by saliva from group O secretors, and according to Morgan's criteria would be classed as true anti-O. This anti-H serum had a macroscopic titre of 1:4 in saline and was used undiluted. For reasons of economy the agglutination-inhibition tests were performed on clear glass slides (four inches by three inches), divided into 24 rectangular compartments with enamel paint.

To one small drop of anti-H serum was added one drop of saliva diluted 1:4 in saline, and the two reagents were well mixed. The slides were then placed in a moist chamber and allowed to stand at room temperature for thirty minutes. One drop of a 2·5% suspension of group O, once-washed cells was then added to each test mixture. The slides then remained in the moist chambers at room temperature for a further period of thirty minutes, after which the mixtures were examined for the presence or absence of agglutination.

It was found that saliva samples from group A and group B individuals gave clear-cut results in all cases. One sample from an A_2B individual showed complete inhibition with anti-B serum but only partial inhibition with anti-A serum. Random saliva samples from A or B secretors gave complete inhibition in dilutions up to 1:512, while random saliva samples from non-secretors showed no (or at the most only slight) inhibition when tested undiluted.

Saliva samples from group O secretors were found to contain the inhibitory substance in much lower titre. The original trial tests were carried out with saliva diluted 1:10, and many cases of partial inhibition were noted. Some of these were still doubtful when the tests were made with saliva diluted 1:4; but we were satisfied to class these subjects as secretors, since their undiluted saliva gave practically complete inhibition. In comparison, it was observed that a group of non-secretors gave no trace of inhibition under the same conditions. The use of undiluted saliva as a routine would appear to be satisfactory with the sample of anti-H serum which we used in these tests. None of the specimens of group O saliva titrated had a titre greater than 1:10 against the weak anti-H serum used.

The tests for Le^a blood reactions and salivary secretion were performed independently in separate laboratories, and the individual results were not known until the final comparisons of results were made. However, initial experience had been gained by us over a number of years, both in Le^a blood tests and in inhibition of agglutination techniques with saliva and other body fluids.

Results and Discussion.

The percentages of Le(a+) in the sexes observed in the present series (Table II) were 25·6 for males and 28·7 for females. The difference (3·1%) is not statistically significant ($\chi^2 = 1{\cdot}156$, $n = 1$, P is 0·2 to 0·3).

The percentage of 26·5 Le(a+) among 1123 individuals tested in Australia is higher than that found in England

TABLE II.

The Le^a Blood Group Distribution in Male and Female White Australians According to A B O Blood Groups.[1]

Sex.	Group O.		Group A_1.		Group A_2.		Group B.		Group AB.		Totals.	
	Number Tested.	Number Le(a+) and Percentage.	Number Tested.	Number Le(a+) and Percentage.	Number Tested.	Number Le(a+) and Percentage.	Number Tested.	Number Le(a+) and Percentage.	Number Tested.	Number Le(a+) and Percentage.	Number Tested.	Number Le(a+) and Percentage.
Males	348	101 (29·0)	238	55 (23·1)	73	19 (26·0)	95	21 (22·1)	42	8 (19·0)	796	204 (25·6)
Females	152	45 (29·6)	95	25 (26·3)	22	5 (22·7)	43	16 (37·2)	15	3 (20·0)	327	94 (28·7)
Totals	500	146 (29·2)	333	80 (24·0)	95	24 (25·3)	138	37 (26·8)	57	11 (19·3)	1123	298 (26·5)

[1] There is some degree of selection within the A B O blood groups.

(22·2%), Denmark (20·0%) and Norway (21·75%), in smaller series. (See Table IV.)

In view of the correlation between the Lewis (Le^a) reactions and the ability of the individual to secrete A, B or H group-specific substances, one might expect to find some relationship between the Le^a reactions and the A B O blood groups. Other workers have found no such relationship, and the present series confirms that the Le^a reactions are independent of the blood groups. The distribution of Le^a amongst the blood groups as shown in Table II when examined statistically yields a value for χ^2 of 4·5, which when $n = 4$ indicates that P is 0·3, and that the observed differences between the blood groups are most likely due to chance. For example, the frequency of Le(a+) in group O was found to be 29·2% as against 24·4% for the remaining groups. This difference is not significant ($\chi^2 = 3·281$, P is 0·07).

TABLE III.

Correlation Between the Le^a (Lewis) Blood Group and A, B or H Salivary Secretion in White Australians.

Blood Group.	Number of Blood and Saliva Samples Tested.	Le(a+),[1] ss.	Le(a+), S.	Le(a−), ss.	Le(a−),[2] S.
O	77	22	0	0	55
A_1	84	19	0	1	64
A_2	16	5	0	0	11
B	19	6	0	0	13
AB	7	1	0	0	6
Totals and (percentages) ..	203	53 (26·1)	0	1 (0·5)	149 (73·4)

[1] Le(a+) = agglutination of blood with anti-Le^a serum; ss = non-secretor of A, B or H substance in saliva.

[2] Le(a−) = no agglutination of blood with anti-Le^a serum; S = secretor of A, B or H substance in saliva.

Table III shows the correlation between the Le^a blood group and the ability of the individual to secrete A, B or H substances in saliva. In all, 203 corresponding blood and saliva samples were tested, and of these subjects 53 (26·1%) were Le(a+) and non-secretors (ss), 149 (73·4%) were Le(a−) and secretors (S). Only one exception (0·5%) was found in the series; an individual of subgroup A_1, N (anti-S−), R_1r, was found to be Le(a−) and a non-secretor. Several repeated tests were performed on fresh blood and saliva samples with the same results.

This series presents further confirmation of Grubb's observation that there is a very close, if not absolute, correlation between Le(a+) red cells and non-secretory saliva, and that the converse relationship between Le(a−) red cells and secretory saliva is very close, though not absolute.

Table IV shows the Le(a+) percentages found in the blood of Caucasians, and indicates the number of samples and the blood groups of the cells tested.

There is little difference in the percentages found in English, Danes, Norwegians and Australians, but the percentage for Australians (26·5) in the largest series is the highest reported.

In Table V an attempt has been made to show the distribution of the secretor and non-secretor types in various races, but the references at our disposal may not be complete.

The lowest percentage of secretors so far reported is in Negroes (61) and the highest percentages are in American Indians (100) and Australian aborigines (94).

All other races recorded here—whites, Japanese, Maoris, Marshall Islanders and Kedayans (Borneo)—all show an S percentage of the order of 70 to 80 approximately.

It would appear that further studies of the Lewis blood group and secretor status in various races may yield valuable genetic data. The results of corresponding Lewis tests on blood, and secretor tests in saliva, may now be used when correlated as a check on the accuracy of the respective tests performed.

TABLE IV.

Le(a+) Percentages Found in the Blood of Caucasians.

Population.	Authors.	Number of Blood Samples Tested.	Blood Groups Tested.	Le(a+) Percentage.
English	Mourant (1946).	96	O	25·0
Danes	Andresen (1948).	238	O	20·0
English	Race *et alii* (1949).	406	O, A, B, AB	22·77
Welsh		33		
American whites		132		
Norwegians ..	Brendemoen (1949).	285	O, A	21·75
English	Grubb and Morgan (1949).	212	O, A, B, AB	22·2
Australian whites	Present survey.	1123	O, A, B, AB	26·5

During the course of this investigation it was hoped to test our large panel of cells with anti-Le^b serum. However, at that time we had not succeeded in finding an example of anti-Le^b serum, nor were we successful in obtaining a sample from overseas.

TABLE V.

Distribution of the Secretor Type in Various Populations.

Population.	Authors.	Number of Individuals Tested.	Percentage Distribution of Types. S.	ss.
Danes	Hartmann.[1]	100	74·0	26·0
Finns	Putkonen.[1]	197	86·3	13·7
Germans (Berlin)	Schiff.[1]	303	78·0	22·0
Japanese	Suzuki.[1]	424	75·7	24·3
Japanese (Nagasaki)	Isizawa *et alii*.[1]	254	79·5	20·5
Poles	Morzycki.[1]	88	79·4	21·6
American whites (New York).	Schiff.[1]	74	82·4	17·6
American whites (New York).	Wiener.[1]	130	82·0	18·0
American Negroes (New York).	Schiff.[1]	178	61·2	38·8
American Indians "Ute" (Utah).	Matson and Piper (1947).	79	100	0
American Indians "Navajo" (New Mexico).	Boyd (1948).		100	0
English	Grubb and Morgan (1949).	212	76·9	23·1
Australian whites	Present survey.	203	73·4	26·6
Australian aborigines.	Preliminary data only.[2]		94	6
Maoris	Preliminary data only.[2]		75	25
Marshall Islanders	Preliminary data only.[2]		72	28
Kedayans (Borneo)	Preliminary data only.[2]		84	16

[1] From A. S. Wiener (1943), "Blood Groups and Transfusion", Third Edition, page 328.

[2] Papers in preparation.

ACKNOWLEDGEMENTS.

We are grateful to Miss Lilian Murray and Miss Frieda Lottkowitz, who collected all the blood and saliva samples tested in this survey, and who kept perfect records of the individual samples.

SUMMARY.

1. The literature relevant to the Lewis blood group and the secretor types in man has been reviewed.

2. A total of 1123 blood samples from unrelated white Australians has been tested with anti-Le^a serum, and 298 (26·5%) were found to give positive results.

3. The Lewis blood group in this large series has been shown to be independent of the A B O blood groups and of sex.

4. A total of 203 corresponding blood and saliva samples has been tested, and close correlation has been obtained between the Lewis and secretor status. Fifty-three (26·1%) individuals were Le(a+) and non-secretors of A, B or H substances, 149 (73·4%) were Le(a–) and secretors, and the only exception (0·5%) was Le(a–) and a non-secretor.

5. Tables have been prepared showing the Le(a+) percentages found in the blood of Caucasians, and the secretor type in various populations.

6. A simple technique for performing Le^a tests has been described, and reliable results have been obtained on blood samples stored in a suitable glucose-citrate preserving fluid at 5° C. for periods up to six months.

7. The Le^a tests on blood and the A B H secretor tests on saliva are now being used in genetic studies on races in the Pacific.

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ÆTIOLOGY OF DIABETES MELLITUS.[1]

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THE ætiology of *diabetes mellitus* presents a number of complicated and contradictory problems, and as the understanding of any subject is usually aided by a knowledge of history, it is appropriate in opening this discussion to consider how our knowledge has developed and how our opinions have changed.

The clinical picture of diabetes was described before the Christian era and was named by Aretæus (A.D. 30 to 90) (Schnee, 1889). Galen a century later was the first to attempt an explanation of the symptoms and suggested that there was a weakness of the kidneys, which could not hold back water. In his opinion the urine consisted of unchanged drink. Avicenna (980-1037) (Dinguizli, 1913) regarded diabetes as a primary disease, but considered that it could arise secondarily to some other disease. With amazing foresight he stated:

> In this disease, the liver is affected and its role of provider of heat is disturbed in consequence of the exaggeration of organic combustions. . . . The relations between the kidney and the liver become irregular, in that the kidney attracts the humours from the liver in greater quantity than it is able to retain them.

The sweetness of diabetic urine, first noted by Susruta in the sixth century (Bose, 1907), was also observed by Avicenna, but seven hundred years elapsed before Willis, in 1675, again emphasized this fact (Willis, 1679). Sydenham (1624-1688) considered that the nutritive elements of the blood were not properly prepared for assimilation and that for this reason "they pour through the kidneys and the flesh and strength melt away". The hereditary character of the complaint was first noticed by Morton (1698). Dobson (1776) proved the sweetness of diabetic urine to be due to sugar. He also observed the sweetness of the blood serum and assumed that there was an excessive accumulation of sugar in the bloodstream, which he thought was formed by some abnormal fermentation of the body. The first association of diabetes with pancreatic disease is attributed to Cawley (1788), who discovered calculi in the pancreas at autopsy on a diabetic patient. However, he regarded diabetes as a disorder of the kidney. Cullen (1709-1790) in 1769 regarded diabetes as a disease of the nervous system. He reported one instance of diabetes in which the urine was "perfectly insipid" and commented on the rarity of this finding. It was Cullen who first added the adjective "*mellitus*" to the name of the disease.

The growth of chemical knowledge in the later part of the eighteenth and early nineteenth centuries paved the way for Claude Bernard (1887), who discovered glycogen and described the glycogenic function of the liver. He suggested that the liver supplied sugar to the circulation from its glycogen store in the intervals between digestion. He produced glycosuria by puncture of the fourth ventricle, thus supporting the earlier conception of the nervous origin of glycosuria. He also postulated the formation of sugar in the body from non-carbohydrate sources. Bouchardat (1806-1886) in 1875 observed hypertrophy of the stomach and atrophy of the pancreas at autopsy on a diabetic patient, and was the first to suggest an influence of the pancreas in the causation of diabetes. In 1846 he attempted unsuccessfully to produce diabetes in a dog by removal of the pancreas. Lancereaux (1888), a pupil of Bernard, attempted the separation of diabetes into two groups, that associated with emaciation, which he assumed to be due to a gross pancreatic lesion and which he termed *diabète maigre*, and that associated with obesity supposedly not pancreatic in origin, which he termed *diabète gras*.

The occurrence of diabetes in dogs following pancreatectomy was accidentally observed by von Mering and Minkowski (1889-1890) in the last decade of the nineteenth

[1] Part of a symposium on *diabetes mellitus*, Section of Medicine, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

century. This discovery, which was to dominate medical opinion on the ætiology of diabetes for the next thirty years, emphasized an earlier observation of Langerhans (1902) on the existence of certain groups of island cells whose function appeared to be unrelated to those of the pancreatic parenchyma. Opie in 1901 discovered degenerative changes in these cells in human patients suffering from diabetes. So there developed the hypothesis which was clearly expressed by Woodyatt (1909) in these words:

> Diabetes mellitus is a disease in which the body has in part lost its ability to utilise sugars. Sugar arrives at the point where it should burn, but fails to do so, and accumulating in the blood creates an hyperglycæmia. Disregarding accessory facts which may play a part, we can say that ultimately the failure of sugar combustion in diabetes mellitus depends upon the lack of "a something derived from the pancreas".

This view received general acceptance, and within the next decade Allen's classical experiments and his pioneering work on the dietary management of the complaint led him to the following conclusion:

> . . . the status of the islands of Langerhans as an internal secretory organ and as the seat of the specific diabetic disturbance is now as firmly established as any fact in physiology or pathology.

Allen (1919) was convinced by the results of his experiments that diabetes arose solely from pancreatic dysfunction, and referred to diabetes as "a unified entity, rather than a disjointed symptom complex". This happy conclusion failed, however, to withstand the weight of clinical experience of the past thirty years.

Stimulated by the apparent failure of function of the islet cells, workers made repeated attempts during the first two decades of this century to isolate an extract which might influence the course of the disease (Zuelser, 1907). All such efforts failed until the brilliant work of Banting and Best in 1922 produced a satisfactory extract. The remarkable effects of this hormone, insulin, and the amazing and universal improvement shown by human patients when treated with it lent enormous support to the pancreatic theory of origin of the disease. It seemed certain that *diabetes mellitus* arose as a result of a quantitative deficiency of insulin, and that once the cause of the pancreatic dysfunction was discovered a cure could be anticipated.

The isolation of insulin, apart from its incalculable value in clinical medicine, stimulated a large amount of clinical and experimental work, which is now turning opinion away from Allen's conception of the primarily pancreatic origin of the disease and even from the idea that it is a single disease entity. Careful studies of autopsy material from patients who have died from diabetes have failed to show any characteristic changes in the islet cells in many instances (Warren, 1938). Diabetes seldom occurs either during the course of or as a sequel to acute pancreatitis (Warfield, 1927; Downie, 1932). Assays of the insulin content of the pancreas from diabetic patients have on occasions yielded normal values (Scott and Fisher, 1938). Recently total pancreatectomy has been performed on human patients suffering from carcinoma of the pancreas (Rockey, 1943). It has been found that diabetes so produced is controlled by daily insulin dosages of approximately forty units. It is a common clinical experience to find that patients may require much larger doses than this to control their condition. In these cases at least it seems that something other than a primary quantitative failure of insulin is responsible (Smelo, 1948).

The role of the various ductless glands has provided a fertile field for speculation and experimentation (Mirsky, 1946). In 1928 Houssay showed that the diabetes which develops after hypophysectomy and pancreatectomy in a dog is materially different and less severe than that which follows pancreatectomy alone (Houssay *et alii*, 1929). During the third decade of this century much interest was shown in pituitary function, and the control of many bodily functions was proved to be maintained by an oscillatory equilibrium between contrary-acting hormones. In some instances at least this balance appears to be controlled by the pituitary gland. Young (1937) showed that the daily injection of fresh crude extracts of the anterior pituitary lobe, if continued for two or three weeks, produced permanent diabetes in the dog. It is interesting that this effect is not found in puppies or in some other adult species. The effects of such pituitary extracts on the adult dog are prevented by the simultaneous administration of large doses of insulin (Haist, Campbell and Best, 1942). Lukens confirmed these findings in cats (Lukens, Dohan and Wolcott, 1943), and showed that low-calorie, high-fat diets also nullified the effects of pituitary extracts. He also showed that, by treating pituitary diabetes with phlorizin before atrophy of the islets occurs, the process can be reversed. These observations led Lukens to emphasize the importance of hyperglycæmia, and he suggested that the level of the blood sugar may be an essential factor in the pathogenesis of diabetes.

Diabetes has been induced in partially depancreatized animals by the injection of adrenal cortical steroids (Ingle, Sheppard, Kuizenga and Evans, 1945), and cortical extracts will aggravate diabetes in adrenalectomized depancreatized animals. Recently a transient diabetic state has been induced in human volunteers by the repeated daily injection of adrenocorticotrophic hormone (Conn, Louis and Wheeler, 1948). Thyreoid secretion has also some influence. Houssay (1944) has induced diabetes in partially depancreatized animals by the exhibition of thyreoid extract. The simultaneous administration of insulin to such animals prevents the development of diabetes.

Alloxan, a purine derivative which apparently is not normally found in the human body, has been shown to produce a rapid and selective death of the cells of the islets of Langerhans (Jacobs, 1937; Dunn, Sheehan and McLetchie, 1943). This discovery has proved to be of considerable value in experimental work, but its relationship to the ætiology of human diabetes is still unknown.

The isolation of insulin naturally provoked inquiry into its mode of action, but it is still uncertain how it acts or where in the complicated chain of carbohydrate metabolism it exerts its influence (Bouckaert and de Duve, 1947). Many of these reactions would seem to be reversible and to be controlled by contrary-acting regulators both enzymatic and hormonal. Insulin is thought to influence the disposal of sugar by the peripheral tissues and the liver, to regulate the level of the blood sugar and to control the formation and breakdown of glycogen. It is also believed to exert some influence on the fixation of amino acids and on the regulation of hepatic ketogenesis. Diverse though these functions may appear to be, it is possible that they reflect the consequence of a single catalytic influence on various basic enzyme systems. This is supported by the work of Cori (1945-1946), who has demonstrated that insulin abolishes the effects of pituitary and adrenal cortical extracts in depressing the rate of the fundamental hexokinase reaction in the initial stage of the breakdown of glucose 6 phosphate.

Soskin (Soskin *et alii*, 1938) has emphasized the importance of the level of the blood sugar and has developed a theory of its regulation by hormonal control. He suggests that the blood sugar value at any given moment reflects the balance between formation of sugar by the liver and its disposal by the peripheral tissues (Soskin *et alii*, 1938; Soskin, 1947). While this conception of a homœostatic mechanism influencing the liver to maintain a constant level of the blood sugar is attractive, no suggestions have been made so far concerning the factors which might disturb such a mechanism and permit an abnormally high level of blood sugar. It is possible that such an alteration, whatever be its cause, could make an increased demand for insulin which in time would be reflected in functional, if not in structural, exhaustion of the pancreas.

The influence of heredity presents another perplexing problem in the ætiology of diabetes. The more carefully the family history of patients is studied, the more important it becomes (Barach, 1949). White (White, Joslin and Pincus, 1934) has stated that 25% of the entire population of the United States of America may be carriers of diabetes, and that this tendency is inherited as a Mendelian recessive characteristic. Wilder (1941) has suggested that sundry apparently unrelated factors may precipitate the

onset of diabetes in a susceptible individual. Of these he considers trauma, shock, infection and pregnancy to be the most important.

The incidence of *diabetes mellitus* by age and sex also poses an unanswered question. It is uncommon before the age of thirty years and its incidence is approximately equal in the two sexes. In the later age groups it occurs more frequently and is found predominantly in females. In general the clinical course and symptoms are more severe in the earlier age groups.

The association of obesity with diabetes, particularly in middle age, has been known for a long time. Joslin (Joslin *et alii*, 1946) has emphasized this and refers to "pre-glycosuric obesity". Within the past decade it has been shown that in some instances symptoms disappear and the glucose tolerance test resumes a normal pattern if a patient's weight is reduced (Newburgh and Conn, 1939). So far this is the only type of patient in whom a cure can occasionally occur. This observation is of importance, as it appears to contradict any idea of pancreatic exhaustion as a primary factor in ætiology (Lawrence, 1946). Another suggestion of a pre-diabetic phase arises from the observations of Barns and Morgans (1948), who examined the fœtal mortality rate in a group of women who subsequently developed recognizable diabetes. Their figures show a high fœtal mortality comparable with that which occurs in pregnancy in known diabetic women. They submit that this is evidence of some endocrine imbalance occurring before diabetes can be recognized by clinical means.

In 1936 Falta, after studying the response of diabetic patients to insulin, suggested that certain patients appeared to be more sensitive to its action than others. Himsworth (1935) at about the same time also suggested a differentiation into insulin-sensitive and insulin-insensitive groups. He (1949) has recently reemphasized this conception and has suggested that *diabetes mellitus* is not a single disease entity, but it is to be regarded as a syndrome which may develop from any one of several causes, the one essential feature of the syndrome being an elevation of the blood sugar level above the limits which are regarded as normal. He considers that the causes of abnormal hyperglycæmia fall broadly into two groups, although he admits that there are several other types which are not yet capable of classification. One group comprises those cases which result from a primary deficiency of insulin or from an inhibition of insulin resulting from overfunction of the anterior lobe of the pituitary gland (insulin-sensitive). The second group includes the abnormal hyperglycæmias of obesity (insulin-insensitive). He emphasizes that, irrespective of the primary cause, abnormal hyperglycæmia, which is common to both groups, can lead to islet damage and secondary insulin deficiency. This concept is a stimulating one and offers a possible answer to the clinical improvement which follows the intelligent use of insulin in almost all cases. This has up to now appeared difficult to reconcile with the results of various experimental observations.

Conclusion.

In conclusion, the experience of the past thirty years has swung medical thought and opinion away from Allen's view that diabetes arises as a result of a primary pancreatic deficiency. The one essential feature of *diabetes mellitus* is abnormal hyperglycæmia, which may arise, at least in some instances, from an increased utilization or destruction or inhibition of insulin rather than from a primary decrease in its production. Much remains to be discovered; but at the present time *diabetes mellitus* is better regarded as a symptom-complex resulting from any one of a number of causes than as a disease *sui generis*.

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PATHOLOGICAL ASPECTS OF DIABETES.[1]

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IN the time available it is virtually impossible to discuss more than three facets of the pathology of diabetes. I propose, therefore, to select three that are not so widely known and recognized as the more extensively described features. In the latter group I refer to changes in the arteries, fatty changes in the liver and the changes described in the pancreas itself. The three conditions selected are the presence of glycogen in the liver cell nuclei, and lesions that are seen in the glomeruli and papillæ of the kidney—conditions which will not be found described in some of the standard text-books.

These changes, if looked for, occasionally lead to the correct pathological diagnosis in cases in which diabetes may not have been suspected clinically—this applies principally to death in coma.

Intranuclear Glycogen.

My interest in intranuclear glycogen was first stimulated by Dr. John Perry, when we were working together at the Walter and Eliza Hall Institute on liver biopsy material. The same changes were originally described by Meixner in 1906 and elaborated by Best in the following year. On ordinary hæmotoxylin and eosin staining the intranuclear glycogen is not seen, but the nuclei nonetheless have quite a characteristic appearance. They appear larger than normal ("bloated" was the original German description), and the nuclear membrane is more prominent. The best description is "halo nuclei". The distribution of these halo nuclei is not even throughout the section, but rather do they occur in groups. In some instances they may be found near areas of fatty change, but their presence is not necessarily related to the fat.

Staining with Best's carmine shows these nuclei to contain a pink granular material dissolved by human saliva. This may appear as a single clump of glycogen or as one or more granules. If there is more than one, often one sees a larger central granule with smaller peripheral granules. It seems that the glycogen appears first as one or more granules which gradually coalesce, at the same time displacing nuclear material to the periphery of the nucleus.

These glycogen-containing nuclei bear an inverse relationship to the cytoplasmic glycogen. As the latter disappears the former increase. Sometimes intranuclear glycogen may be seen in cells containing some glycogen in their cytoplasm. With recovery and increase in cytoplasmic glycogen, the nuclear changes disappear.

This appearance is typical of the liver in *diabetes mellitus*. Though the "halo nuclei" have been seen in other conditions, they are never so intense and usually a search has to be made for them. I have seen occasional "halo nuclei" in chronic hepatitis and starvation, while the original German writers described them in congested livers, miliary tuberculosis and amyloid disease. The presence of occasional "halos" is not typical; but when they occur in definite groups diabetes will be found to be the underlying disease.

Intercapillary Glomerulosclerosis.

Intercapillary glomerulosclerosis was first described by Kimmelstiel and Wilson in 1936, and since then numerous reports have been written from all over the world. There has been a great deal of argument as to the specificity of the lesion for diabetes. The consensus of opinion is that when it is present to a definite degree it is indicative of *diabetes mellitus*.

It is recognized by the presence of hyaline material in the glomeruli between the capillary loops. It is commonly present near the periphery of the tuft, and may have as an associated lesion thickening of the afferent arteriole. Sometimes focal masses of hyaline material are seen scattered through the glomerulus, or it may appear as a single large clump occupying up to half the glomerulus. At other times it is scattered diffusely through the glomerulus. The severity of the condition is usually assessed by the relative amount of hyaline material in each glomerulus and the number of glomeruli which are involved.

The nature of this hyaline material has not been finally settled. Fahr at one stage considered it to be amyloid, but later stated that its staining properties were different. This has been confirmed by Henderson and others at the Mayo Clinic. Allan has shown the hyaline mass to consist of strongly argentophile laminated fibres differing in intensity of impregnation and arrangement from hyaline deposits in non-diabetic glomerulosclerosis. Also noted was a resistance to tryptic digest by the "diabetic type" of hyaline deposits which was not seen in the non-diabetic types. There can be no doubt that the severe grade of this condition is specific for diabetes, and when present is just as definite as the finding in pre-insulin days of masses of glycogen in the renal tubules. Lutens and Dohan claim to have found early lesions of this type in dogs rendered diabetic by anterior pituitary extract and examined after five years of diabetes.

The mild form, which is also called the diffuse form (in contradistinction to the severe or nodular form), is regarded by many workers as an early stage of the condition. It can be found in other conditions, such as severe hypertension, in chronic nephritis and as an aging process. An intermediate form between these two has also been described.

Frequency.

It appears that intercapillary glomerulosclerosis occurs in about 17% of all diabetics, being twice as common in females as in males (approximately). It occurs but rarely in the first two decades, and a slow rise in incidence commences in the third decade. The maximum incidence is in the sixth decade, and more severe lesions are found in this age group.

Period of Evolution.

The only light shed on the problem of the period of evolution is a case reported by Derow and Schlesinger. The subject was a woman, aged sixty-one years, who had diabetes for four years before a nephrectomy was performed for suspected neoplasm. Examination of the removed kidney revealed a large renal cyst, but microscopic investigation did not show any glomerular lesions except that 3% of the glomeruli examined were completely hyalinized. Two years later the patient developed severe albuminuria, and she died from renal failure after a further two years. A microscopic examination of the kidney at autopsy showed that 8% of glomeruli were completely

[1] Part of a symposium on *diabetes mellitus*, Section of Medicine, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

hyalinized, but 47·5% were affected by a severe degree of intercapillary glomerulosclerosis and 25% by a moderately severe degree. It is worth noting that the patient developed diabetic neuropathy and retinal lesions at the same time as the albuminuria.

Associated Lesions.

There is no direct clinical relationship between intercapillary glomerulosclerosis and hyalinization of the islands of Langerhans. Treatment of the diabetes does not affect the development of the lesion, which is usually seen in relatively mildly diabetic subjects. The severity of the diabetes does not parallel the severity of the glomerular lesions. Usually diabetes is present for six years or more before the development of renal signs.

Advanced retinopathy, especially of the diabetic type, is consistently associated with glomerular changes. It precedes the latter and is more closely related to the diabetes than to the vascular or renal changes.

Papillary Necrosis.

The association of papillary necrosis and *diabetes mellitus* was first emphasized by Gunther in 1937. However, the first report of the condition was by Friedreich in 1877. The first description of papillary necrosis and diabetes was by Turner in 1888.

That attention has not been given to this entity can be seen from published figures; up to 1947 only 110 cases had been reported, and of these subjects 62 had proven diabetes. From reported series it seems that 12% to 20% of diabetics at autopsy show evidence of pyelonephritis. Approximately one-quarter of these show papillary necrosis—that is, the lesion may be found in about 4·0% of diabetics at autopsy. Against this, in non-diabetics it may be found in only 0·06%, and the great majority of non-diabetics showing this lesion have urinary tract obstruction. As further evidence of this difference is the sex ratio: in diabetics it is two females to one male, but in non-diabetics the female to male ratio is 1:6.

A few words about the clinical picture may help in appreciating the importance of the condition. The symptoms may be fever, hæmaturia and pyuria in the acute forms, even with renal colic due to sloughing and subsequent ureteric passage of a necrosed papilla. In the more chronic forms the picture is that of a resistant urinary tract infection, quite often suddenly becoming worse. Even the appearances at pyelography may be misconstrued, owing to the defect in the calyces leading to the diagnosis of renal tumour or tuberculosis.

The kidneys are usually larger than normal and the necrosis is usually bilateral in diabetics, while it is more commonly unilateral when it occurs in non-diabetics. The degree of necrosis varies from the involvement of the tip only to necrosis of most of the papilla. Sometimes the necrosis may extend into the pyramid and rarely up to the cortico-medullary junction. At other times there may be a separation of the papilla at the line of demarcation from the remainder of the pyramid. In still other kidneys the papilla may have sloughed completely.

Microscopically one can see acute pyelonephritis. The involved papillæ are affected by necrosis of all their elements without inflammatory infiltration. At the line of demarcation there is a cellular zone containing polymorphonuclear leucocytes and round cells, adjoining which is a zone of hyperæmia.

Pathogenesis.

1. Infection. It is apparent that in all cases the condition occurs in association with pyelonephritis. It has been suggested that bacterial toxins are the cause, but the wide variety of the flora rather cancels this out as the sole agent.

2. Circulatory factors. The blood supply to the pyramid is relatively poor, and the infarct appearance of the necrosis at once suggests a vascular origin. As there is no single vessel supplying this area, it would require multiple thrombosis. This has been described in a few cases, but by no means all specimens show it.

3. Mechanical factors. Back pressure on the papillary blood supply has been suggested as a cause of the ischæmia. If this was so, one could reasonably expect to see papillary necrosis more often in cases of hydronephrosis and renal calculi.

4. Role of diabetes. There is no doubt of the importance of diabetes in the production of this necrosis. Exactly how it occurs is not so clear. Harrison and Bailey have shown that bacilluria and pyuria are approximately five times more common in diabetics than in non-diabetics. Menkin holds that there is a difference in the inflammatory process in diabetics due to a local decrease in pH. Finally, there is experimental evidence that disturbance in fat metabolism in animals can reproduce this lesion.

Conclusion.

All the three lesions presented have this fact in common—that while they may be seen in non-diabetics, their presence in a definite, recognizable form may be taken as pathological evidence that the patient suffered from *diabetes mellitus*.

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WHY DIET THE DIABETIC?[1]

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IF you cannot cure a disease—and so far as I know you cannot cure diabetes—the next best thing is to make and keep your patient well, happy and economically efficient; in other words, to render him physiologically, psychologically and sociologically normal. Diabetes is one of the diseases in which that objective can be attained in its entirety in nearly every case.

If you ask many doctors and most laymen what methods are used in the treatment of diabetes, you will be told that there are two, diet and insulin—diet certainly, insulin possibly. It is the purpose of this paper to suggest to you that the two may be reduced to one—insulin.

[1] Part of a symposium on *diabetes mellitus*, Section of Medicine, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

Why diet the diabetic? Put this question to a doctor who is in the habit of prescribing the diet of his diabetic patients. You may get any of the following answers.

1. To avoid the necessity of giving insulin. This is a bad answer. All diabetics, irrespective of age, are better off with insulin. My two oldest diabetics are octogenarians. Both have been tried on orthodox dietetic methods. Both were thereafter switched to a normal diet and a small dose of protamine zinc insulin once a day. Both state definitely that they much prefer the later to the earlier régime.

Apart from the patient's sense of well-being, however, there is something even more important. The so-called "mild" diabetics of middle age, who are in no danger of losing their lives from ketosis and coma, and who are "treated" for years by diet alone, are the people who in later years develop gross arteriosclerosis (peripheral and cerebral), retinitis, cataract and gangrene. Anyone with any extensive experience of these tragic affairs will never treat his diabetics without insulin.

2. To keep the insulin dose as low as possible. There is a curious belief, prevalent amongst doctors and patients alike, that one should always endeavour to keep the dose of insulin as small as possible. A feeling exists that a patient receiving 20 units of insulin per day is in some way better off than one receiving 40 or 60 units. True, the cost is less, though the difference is probably only a penny or two in a day. Otherwise the belief is completely without foundation, and a diabetic who needs 60 units a day is essentially just as fit and stable as one receiving a quarter of that dose.

However, even if there was some physiological justification for the desire to reduce insulin dosage, it must be remembered that no direct relationship exists between the contents of a patient's diet and his insulin requirement. I was able to demonstrate this as long ago as 1932, when, by courtesy of my colleagues, I took over as a going concern the management of 20 diabetics, all of whom were receiving weighed and measured diets and all of whom were on a fairly stable dose of insulin. The protein and fat intake was approximately that of a normal individual. The carbohydrate intake varied from 80 to 140 grammes per day. In each case I left the protein and fat intake unchanged and increased the carbohydrate intake to or above 250 grammes per day. Six months later 18 of the 20 patients needed less insulin, and only one—who had developed cholecystitis—needed more.

This finding opens up the whole complex question of insulin action and its relationship to hepatic insufficiency. Suffice it here to state briefly that insulin is concerned largely with endogenous rather than exogenous metabolism. The traditional statement that so many grammes of glucose (or its equivalent) require so many units of insulin for their metabolism is entirely fallacious and has confused the minds of countless medical students and medical practitioners for many years. It is still doing so.

3. To maintain diabetic stability. This involves the same misconception as the previous answer. Normal people vary their food intake in accordance with their activities, the weather and the state of their alimentary tract. The food requirements of diabetics vary in exactly the same way. Empirically, as I shall show later, diabetics are much more stable if they vary this food intake as a normal person would, rather than if they religiously consume their fixed quota of this, that and the other at the appointed time.

4. To maintain intake of essential foodstuffs. This, after all, has nothing specifically to do with diabetes. Everybody, diabetic or not, requires an adequacy of protein, of vitamins, of essential minerals. He is just as likely to get these from a normal as from an artificially controlled diet.

5. Because diabetics always have been dieted. This, I think, is getting very near the bone. Tradition dies hard, and nowhere harder than in old-established fashions of medical treatment. Before Banting, diet offered the only possibility of modifying in any way the manifestations of the disease. Surely, it is said, it must still have some part in its treatment. Yet, "what was good enough for my grandfather is good enough for me" is not always sound reasoning.

6. To banish or prevent obesity. This at least is good, sound sense. The statistics of the big life assurance companies have shown clearly that the fat man dies earlier than the man of normal girth. He also dies much less comfortably. Irrespective, therefore, of whether your patient is diabetic or not, it is proper to remove his superfluous fat by reducing his caloric intake. In the fat diabetic an additional reason for weight reduction is that excessive fat magnifies insulin requirement beyond all reason.

I therefore agree entirely that fat diabetics should be reduced to normal proportions by suitable modifications of diet.

7. To prevent diabetics from becoming arteriosclerotic. An excessively high fat intake is said to be a predisposing factor to the development of atherosclerosis, although there is as yet no sure knowledge on this point. Excessive fat intake in any event leads to obesity and for that reason alone should not be permitted. My own experience of giving generous diets for over twenty years and practically unrestricted diets for fifteen years is that arteriosclerosis does not develop prematurely in the diabetic receiving such diets who is treated early and adequately with insulin, but does develop in the patient whose treatment has consisted of diet alone or diet *plus* an inadequate amount of insulin.

It will thus be clear that, except on the question of obesity, I remain unconvinced by any of the arguments usually advanced in favour of dieting the diabetic. I prefer to allow my non-obese diabetics to eat normal meals in a normal manner, varying both quantity and quality as the spirit moves them. The amount of insulin is adjusted in accordance with the needs of the individual patient. There is not time here to discuss the details of this adjustment; suffice it to say that the process takes place under my direct supervision for the first two or three weeks, and thereafter is carried out independently by the patient in accordance with the variation in the urinary sugar excretion.

Advantages of Free Diet.

From the physiological point of view patients receiving a free diet become and remain perfectly fit. Psychologically the method has obvious advantages. The sense of being different from others, which leads directly to the development of an inferiority complex, no longer exists. This is of course particularly important in the case of children. In children also the normal opprobrium attaching to a little promiscuous indulgence in carbohydrates no longer exists and the development of a sense of guilt does not occur. The irksome business of going into hospital to learn one's diet does not happen. True, some of the diabetics whom I transfer from a restricted to a free diet are robbed of one of their regular topics of table-talk, but I cannot bring myself to believe that that really matters.

The sociological advantages of a free diet are just as important. The diabetic may eat in home, hotel or restaurant with impunity. He may travel on business or pleasure without let or hindrance and have no worry as to whether he will be able to get his proper diet on the way. He can take a job anywhere. Very important in these days of domestic difficulties, the cook in the home is spared the necessity of preparing separate meals or separate dishes for a single member of the family. All these things matter.

Analysis of Records.

It is one thing to extol the theoretical advantages of a method of treatment. It is much more important to find out whether it works, particularly in such a disease as diabetes, in which practice has appreciably outstripped theory.

I have therefore analysed the records of 191 diabetic patients examined for the first time by me in private practice between April, 1946, when I returned to practice, and

April, 1950. The list includes all the diabetics first examined in private practice during that period for whose treatment I was personally responsible. It does not include diabetics examined only once or twice in consultation. The group includes 76 males and 115 females scattered in age over the decades in the manner demonstrated, and ranging from a year and ten months to eighty-four years, the numbers being greater, as is customary, in the fifth, sixth and seventh decades. The list is as shown in Table I.

TABLE I.
Age Groups of 76 Male and 115 Female Diabetics.

Age Group. (Years.)	Number of Subjects.
1 to 10	5
11 to 20	14
21 to 30	11
31 to 40	10
41 to 50	31
51 to 60	53
61 to 70	48
71 to 80	17
81 to 90	2

In some cases I was the patient's first doctor. More often I had had one or more predecessors. This can be deduced from the record of duration of symptoms prior to the patient's coming under my care (Table II). I have

TABLE II.
Duration of Symptoms.

Years.	Number of Subjects.
Under 1	37
1 to 2	28
2 to 3	10
3 to 5	26
5 to 10	43
10 to 20	33
Over 20	14

not attempted to dissect these figures further, my purpose in quoting them being merely to show that the group is reasonably representative of the disease as it presents itself in its various types and stages to the consultant general physician.

TABLE III.
Daily Dosage of Protamine Zinc Insulin, 128 Cases.

Units.	Number of Cases.
1 to 10	17
11 to 20	49
21 to 40	46
41 to 60	16

It is perhaps of passing interest that I was able to obtain a family history of diabetes in over one-third of the cases—68 out of 191. This is a much higher proportion than I could get fifteen or twenty years ago. It must steadily increase as diabetic males survive to the reproductive age and diabetic females pass successfully through pregnancy.

Of the 191 patients, I judged that 48 were by any standard—functional or æsthetic—too fat. These were placed, with greater or less success, on the reducing diet set out as follows:

Reducing Diet:

Omit completely: butter, cream, dripping, fats and oils, bacon, ham, fried food, cheese, sugar, confectionery, flour, bread, toast, cakes, biscuits, scones, pastry, cereals, porridge, potatoes, bananas, beer.

Let your diet consist chiefly of: fruit, vegetables, meat, fish, eggs and milk.

In my experience patients find it easier to do without a particular foodstuff altogether than to limit their consumption of it. Anybody who has tried to moderate his smoking will appreciate the psychological angles of this question. The important thing in weight reduction is, of course, the weekly weighing. The specific diet is intended as a guide rather than as an inviolable law. The optimal end-point is agreed between the patient and myself, as is the time to be occupied in reaching that happy state. The

TABLE IV.
Combined Insulin (Protamine Zinc Insulin plus Ordinary Insulin), Daily Dosage (44 Cases).

Units.	Number of Cases.
21 to 40	11
41 to 60	20
61 to 100	10
Over 100	3

resultant calculation involves a steady loss of one, one and a half or two pounds per week, and the food intake is controlled by the patient to bring this about. In general it works—sometimes the battle is a stern one.

Patients who are of normal dimensions or underweight are warned of the risks of obesity, but told that so long as they do not grow fat they may eat what they will and

TABLE V.
Ordinary Insulin (Twice a Day), Daily Dosage (19 Cases).

Units.	Number of Cases.
21 to 40	4
41 to 60	6
61 to 100	7
Over 100	2

as they will. It is suggested to them that the eating of a large amount of soluble carbohydrate—sugar or cake—late in the afternoon, though it will not do them any harm, may derange their late afternoon urine test, by which their morning dose is regulated, and therefore is to be deprecated. Provided that the patient appears to have

TABLE VI.
Causes of Admission to Hospital.

Initial. (16 Cases.)		Subsequent. (6 Cases.)	
Condition.	Number of Cases.	Condition.	Number of Cases.
Gangrene	4	Sepsis	2
Sepsis	7	Insulin reaction	1
Cataract	2	Gastro-enteritis and coma	1
Precoma	2	Cerebral vascular accident	2
Stabilization	1		

enough intelligence to eat a diet not lacking in any essential foodstuff, no further restriction of any kind is imposed.

All the 191 patients received insulin. One hundred and twenty-eight patients used protamine zinc insulin once a day, in dosage ranging from eight to 60 units. The dosage is set out in Table III. In general protamine zinc insulin alone was used for patients over the age of forty. Forty-four patients received a combination of protamine zinc insulin and ordinary (soluble) insulin given once a day (Table IV). These were generally patients aged between fifteen and forty years, or patients aged over forty years in whom the disease was unusually acute. The total dosage received by each patient ranged from 28 to 120 units. Two

of the three patients requiring over 100 units were examples of long-standing carbohydrate restriction, a most potent cause of high insulin dosage. The third was a boy who demonstrated the high dosage sometimes required at puberty.

In 19 cases it seemed advisable to use ordinary insulin twice a day (Table V). These were in general children aged under fifteen years, or patients whose diabetes was complicated by some toxic or infective process. Of the two patients requiring over 100 units a day, one was an unstable temperamental menopausal women who also had been starved of carbohydrates for many years. The other was a sick consumptive.

From a fairly extensive study of the records of other clinics, I think it is fair to state that the insulin requirement of these patients does not exceed that of any large group of diabetics treated by diet restriction as well as insulin; indeed, it is my impression that the average dosage is somewhat less. A free diet does not involve increased insulin dosage.

I said earlier that the aim of treatment in diabetes is to render the patient physiologically, psychologically and sociologically normal. A very satisfactory criterion of the efficiency of any regime of treatment is the frequency with which it is necessary to admit its followers to hospital. It must be agreed that diabetics in hospital are neither well nor—as a rule—happy or economically productive.

Of this group of 191 patients, only 22 have at any time been admitted to hospital for the treatment of their diabetes or any complication thereof. The reasons for admission to hospital may be of interest (Table VI). In 16 of the 22 cases the patient was either in hospital or required immediate admission when first examined by me. In four cases gangrene was established. In seven cases there was sepsis of appreciable severity. Two patients were about to undergo operation for cataract. In two instances intercurrent infection in untreated patients caused coma. One patient only of the whole group was admitted to hospital for stabilization, and here the circumstances were exceptional.

> The patient was a girl, aged three years, whose parents had a farm hundreds of miles away. The mother was expecting another child in three weeks. The father could not leave the farm owing to the bush-fire risk. We thought it fair to keep the child in hospital for a couple of months until the parental difficulties were resolved.

Of the six patients who required hospital admission subsequent to coming under treatment, one developed a crop of boils and one an abscess at the site of injection. One had an insulin reaction of considerable severity; mildly psychopathic, he has no idea of what really happened on New Year's Eve and New Year's Day, but recovered consciousness in hospital. One "ran off the rails" and into early coma during an attack of acute gastro-enteritis. The final two had cerebral vascular catastrophes—one thrombosis, one a hæmorrhage—and since arteriosclerosis is commonly listed amongst the complications of diabetes, I have judged it fair to include these in the list.

Of the remaining 169 patients, one can see so little through her retinitis and her cataracts that she can do very little. The 168 others have not had their economic productivity in the home, the office, the factory or the farm seriously interfered with by their diabetes and its treatment.

Pregnancy.

Of this group, nine women have passed safely through ten pregnancies, with the production of eight healthy babies. Of the two unsuccessful pregnancies, one child was stillborn—the mother had been toxæmic in the late stages of pregnancy. In the other case labour was prolonged for two and a half days, and the baby died six hours after birth. In retrospect, it is clear that Cæsarean section should have been performed in this case.

Comment.

It is my submission that these records indicate a remarkable stability and freedom from complications in patients on this regime, and that they provide no support for the opinion that uniformity in the daily caloric intake is necessary for the maintenance of metabolic equilibrium.

The figures quoted are those of a group of patients examined in post-war private practice. My pre-war private patients more than double the total. Similar principles are applied in the treatment of some 50 diabetics under the charge of the Repatriation Department, whom I handle personally, and of about 700 patients attending the diabetic clinic of the Royal Perth Hospital, who are treated under my direction. Similar economic efficiency is attained in both these groups. It is thus fair to say that to my personal knowledge above a thousand Western Australian diabetics—the fat ones always excepted—enjoy freedom to eat as they choose and take no harm thereby.

It has been suggested to me that diabetes in Western Australia may be milder than elsewhere in the Commonwealth. I believe this suggestion to be without foundation. The late Dr. Eric Cooper and I were the two original workers in the (Royal) Melbourne Hospital diabetic clinic from 1926 to 1928. I looked after the diabetics at the Children's Hospital in Melbourne during those two years. I have worked in diabetic clinics in London, in New York and in Boston. Nowhere have I seen any essential differences in the severity of the clinical manifestations of untreated diabetes or in the response to appropriate treatment.

Summary.

Let me endeavour to sum up the situation as I see it regarding the dieting of diabetics in a short series of questions and answers. The questioner is an intelligent layman. The responder is myself:

Question: What is a diabetic?

Answer: A person who cannot in his own body produce enough functioning insulin for his needs.

Question: Is there anything else fundamentally wrong with him?

Answer: I do not think so.

Question: Then if you give a diabetic enough insulin to make up the deficiency, does he not thus become a normal person?

Answer: To the best of my knowledge, yes.

Question: Then why not give him a normal diet?

Answer: I just don't know.

DIABETIC PREVALENCE IN NEW SOUTH WALES.[1]

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IT is of some interest to know the prevalence of any chronic disease in a community. Firstly, if we had a good idea of the prevalence—that is, of the number of persons suffering from the disease at a point of time—we might be able to guess at approximate case-mortality rates, using the recorded deaths from the official statistics. Secondly, it would be of some administrative importance to be able to make a forecast, with the aid of prevalence rates, for they would lead to an estimate of the clinic accommodation likely to be required at any future date. Thirdly, the prevalence rates would give rather more exact information than we possess at present of the natural history of the disease. We shall be interested in this paper only in attempting to find the prevalence rates of diabetes in New South Wales.

[1] Part of a symposium on *diabetes mellitus*, Section of Medicine, Australasian Medical Congress (British Medical Association), Seventh Session, Brisbane, May-June, 1950.

Methods of Obtaining the Prevalence Rates in Diabetes Mellitus.

Two prevalence rates for diabetes may be estimated, the prevalence of known diabetics or the prevalence of previously known and unknown subjects. In general, except in sources (iii) and (vi) below, we shall be dealing only with the prevalence of known diabetes. There are several sources of information concerning the number of diabetics in the community: (i) the attendance of diabetics at clinics; (ii) the issue of special ration cards to diabetics during periods of rationing; (iii) physical examinations carried out in connexion with entry into the armed forces or admission to civil posts, or examinations for life assurance; (iv) census *questionnaires*; (v) special *ad hoc* surveys; (vi) the exhaustive clinical examination of a community.

TABLE I.

The Completeness of Application of the Diabetics in New South Wales for the Special (Diabetic) Ration Cards.

Year of Application.	Number of Applicants.			
	Males.	Females.	Sex Unstated.	Total.
June, 1943, to June, 1944	2378	3977	35	6390
June, 1944, to June, 1945	2828	5416	—	8244
June, 1945, to June, 1946	2631	5383	—	8014

The Number of Patients Attending Diabetic and Other Clinics.

The number of patients attending diabetic clinics can give us some idea at least of the minimum number of diabetics in the community. We cannot know what percentage of the diabetics in the community attends the clinics, nor whether there is any special age or sex selection. Here, we shall use only the clinic material as a comparison for the age distribution of the ration card holders.

TABLE II.

The Number of Applicants for Extra Butter Issue in New South Wales in the Period June 5, 1944, to June 3, 1945.[1]

Age Group. (Years.)	Applicants.	
	Males.	Females.
0 to 14	36	50
15 to 19	43	44
20 to 29	152	141
30 to 39	256	431
40 to 49	397	645
50 to 59	697	1408
60 to 69	550	1312
70 to 79	267	630
80 and over ..	49	147
Age unspecified ..	381	608
Total ..	2828	5416

[1] Data by the courtesy of Mr. E. Ford, the Deputy Commissioner for Rationing in New South Wales.

The Holders of Special (Diabetic) Ration Cards.

It seemed possible that most diabetics might be expected to apply for the special ration cards in the war years. These cards entitled them to more meat and butter but less sugar than the ordinary ration card. A lower limit might thus be set to the number of known and diagnosed cases of diabetes in the population. A medical certificate was required for the initial application, and so there appears little reason to doubt that these persons were, in fact, diabetic. We shall therefore consider in detail the number of applications in New South Wales in the period June, 1944, to June, 1945. We may note that each applicant was required to reapply each year, so that the number of applicants is also the number of the holders of the special ration cards. In Table I is given the total number of applicants in three successive years for New South Wales.

In the first twelve months, it would appear that all diabetics did not apply, but in the next two periods the numbers are practically equal. Of course, this does not mean that all diabetics had applied in these years. We have no way of determining how many diabetics did not apply because they were in institutions, did not worry about their diet or lived in those parts of the State where access was easy to unrationed butter and meat. All we can infer is that the estimate is a minimum for the number of known diabetics in New South Wales. In Table II are given the numbers of the holders of the special ration cards by age and sex.

TABLE III.

The Prevalence of Diabetes in New South Wales as Measured by the Number of Holders of Special (Diabetic) Ration Cards per Thousand of the Population of the Same Age and Sex.[1]

Age Group. (Years.)	Applicants per Thousand in New South Wales.	
	Males.	Females.
0 to 14	0·1	0·1
15 to 19	0·3	0·4
20 to 29	0·7	0·7
30 to 39	1·4	2·3
40 to 49	2·3	3·8
50 to 59	5·8	12·4
60 to 69	7·2	17·9
70 to 79	7·1	17·4
80 and over ..	6·2	16·5

[1] These figures understate the diabetic prevalence by some 11% or 12% in both sexes. Probably the understatement is greatest at the higher ages. No attempt has been made to distribute the "age unspecified" group.

In Table III, we have obtained a rate by dividing the number of holders at each age by the corresponding number of persons in New South Wales as enumerated at the Census of the Commonwealth of Australia of June 30, 1947. It will be noted that the rates are much below the rates obtained at Oxford, Massachusetts, by Wilkerson and Krall (1947), but are of the same order of magnitude as those determined for the United States in the National Health Survey of 1935-1936 and those for the State of Massachusetts in 1929-1931, which are quoted in Table IV, from Spiegelman and Marks (1946).

TABLE IV.

The Prevalence of Diabetes in the United States of America as Measured in Two Surveys (cited from Spiegelmen and Marks, 1946).

Age Groups. (Years.)	Males (per Thousand).		Females (per Thousand).	
	National Health Survey, 1935–1936.	Massachusetts Survey, 1929–1931.	National Health Survey, 1935–1936.	Massachusetts Survey, 1929–1931.
40 to 49 ..	3·1	4·2	5·5	5·0
50 to 59 ..	6·8	6·6	13·1	15·1
60 to 69 ..	12·8	10·3	21·8	17·2
70 to 79 ..	15·8	10·4	22·7	19·0
80 and over ..	11·2	10·0	11·4	14·0

It is therefore evident that the estimates of the diabetic population in New South Wales suggest that the prevalence of known diabetes in New South Wales is of the same order as that in the United States of America, which is in keeping with the mortality findings (see Lancaster and Maddox, 1950).

Diabetic Prevalence as Estimated by Routine Physical Examinations.

Diabetic prevalence might be estimated from routine physical examinations such as are conducted by life assurance companies, the civil service and so on, at entry. The

difficulty that arises is bias, because such groups of examinees are almost invariably selected groups.

Census Questionnaires to Estimate the Prevalence of Diabetes or Other Chronic Disease.

At the censuses in Australia before 1947, there was usually a question directed towards the estimation of chronic diseases, believed to be of administrative importance. It would be possible to expand this question in future censuses to include the more important chronic diseases, such as diabetes, rheumatism, tuberculosis, deafmutism and blindness. It may be desirable not to have this question answered with the general *questionnaire*, but to use specially trained enumerators to obtain the information required in a sample of the population. This type of procedure is routine practice in the Bureau of the Census of the United States of America and has also been used in India.

TABLE V.

A Table to Show the Approximate Equality of the Age Distributions of the Holders of the Special Ration Cards and the Clinic Patients from the Diabetic Clinic of the Royal Prince Alfred Hospital, Sydney; the Percentages of Diabetics by Age Groups.

Age Group. (Years.)	Percentage of Persons in the Age-Group among			
	Ration Card Holders in New South Wales, 1944–1945.		Diabetics of the Diabetic Clinic of the Royal Prince Alfred Hospital, 1950.	
	Males.	Females.	Males.	Females.
0 to 14 ..	1·5	1·0	2·7	1·7
15 to 19 ..	1·8	0·9	1·2	1·2
20 to 29 ..	6·2	2·9	5·5	5·3
30 to 39 ..	10·5	9·0	8·2	5·2
40 to 49 ..	16·2	13·4	13·7	11·0
50 to 59 ..	28·5	29·3	23·1	25·6
60 to 69 ..	22·5	27·3	29·0	35·4
70 to 79 ..	10·9	13·1	13·7	13·3
80 and over ..	2·0	3·1	2·7	1·3

Special Ad Hoc Investigations.

The National Health Survey in the United States of America was carried out in the years 1935 and 1936 on a sampling basis, and many data on the chronic diseases were collected. Such surveys are expensive, and it is necessary to use some sampling technique. However, if several chronic diseases were investigated simultaneously, the costs might be shared between several different organizations.

The Exhaustive Clinical Examination of a Community for Diabetes.

Such exhaustive surveys have rarely been carried out. They are, indeed, practicable in some populations only in the time of war, although with those in reserved occupations, known invalids and so on not being examined, bias is likely to arise. It is to be regretted that no studies of such a nature were carried out in Australia in the recent war. The survey of Wilkerson and Krall (1947) was an attempt at a complete survey of a population, which, however, was limited in extent.

Discussion.

In Table V is given the age distribution in percentages for each sex. It is seen that the age distribution of the clinic patients from the diabetic clinic of the Royal Prince Alfred Hospital is approximately the same as that of the ration card holders. We may note that the present prevalence rates measured in the American population would be greater than in 1935-1936, partly owing to improved methods of diagnosis, partly owing to more successful treatment which results in a lengthened expectation of life for those in the later years. The tables show that if these factors are borne in mind, we may consider the diabetic prevalence in New South Wales to be somewhat less than that in the United States of America.

Acknowledgements.

This paper is published with the permission of Dr. A. J. Metcalfe, Director-General of Health, Commonwealth of Australia. I wish to thank Mr. E. Ford, Deputy Commissioner of Rationing in New South Wales, for the data of Tables I and II, and Dr. J. Kempson Maddox for the data from the diabetic clinic of the Royal Prince Alfred Hospital, Camperdown.

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AN ANTI-INSULIN FACTOR IN THE PLASMA OF DIABETIC PATIENTS.

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FROM time to time a number of factors have been postulated as ætiological agents in *diabetes mellitus*. Amongst others are failure of the islets of Langerhans to produce insulin, hyperfunction of the anterior part of the pituitary gland, increase in neoglucogenesis by the liver, and abnormal destruction of insulin by the tissues.

It appeared that alloxan diabetic, hypophysectomized, adrenalectomized (A.D.H.A.) rats (Bornstein, 1950*a*) would be suitable preparations with which to show the presence or absence of any anti-insulin factors in plasma freshly obtained from diabetic patients. Such preparations can be used to assay minute quantities of insulin, being sensitive to as little as 0·05 milliunit of insulin, and in them minute amounts of crude pituitary extracts and adrenal extracts produce a considerable rise in blood sugar level.

The steps of the technique (Bornstein, 1950*a*) of the experiment were as follows:

1. Groups of eight A.D.H.A. rats were used in each instance. The mean fall in blood sugar concentration resulting from the administration of 0·2 milliunit of insulin (I) was determined.

2. An amount of 0·5 millilitre of plasma, prepared immediately after taking of blood, was injected into each animal and the plasma insulin level determined.

3. The animals were again tested for sensitivity to insulin at four and seven days after the injection of the plasma taken from a diabetic patient, and at weekly intervals thereafter.

In order to check the observed effect, Gemmill (1941) experiments at a substrate glucose level of 200 milligrammes per 100 millilitres were performed with some of the animals.

[1] Working under a full-time grant from the National Health and Medical Research Council.

The patients studied were in three groups: (*a*) 11 unselected, untreated, diabetic patients; (*b*) four unselected, stable, diabetic patients; (*c*) two insulin-resistant diabetic patients.

They are the same patients whose plasma insulin levels were reported previously (Bornstein and Trewhella, 1950*a*).

Results.

The results obtained are shown in the tables below.

Unselected, Untreated, Diabetic Patients.

The results obtained with unselected, untreated, diabetic patients are shown in Tables I to XI.

CASE I.—J.S., a female patient, aged forty-one years, had a blood sugar content at the time of experiment of 486 milligrammes per 100 millilitres. The results obtained with rats of group A_2 are shown in Table I.

TABLE I.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
8.7.49	0·2 milliunit insulin.	42±9
12.7.49	0·5 millilitre patient's plasma.[1]	1±2
16.7.49	0·2 milliunit insulin.	3±4
20.7.49	0·2 milliunit insulin.	3±4
27.7.49	0·2 milliunit insulin.	5±5
3.8.49	0·2 milliunit insulin.	10±6
10.8.49	0·2 milliunit insulin.	35±7

[1] The result indicates that the plasma insulin content=0.

CASE II.—J.L., a male patient, aged twenty-eight years, had a blood sugar content at the time of experiment of 402 milligrammes per 100 millilitres. The results obtained with rats of group AB_1 are shown in Table II.

TABLE II.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
6.6.49	0·2 milliunit insulin.	40±11
10.6.49	0·5 millilitre patient's plasma.[1]	2± 4
14.6.49	0·2 milliunit insulin.	1± 3
17.6.49	0·2 milliunit insulin.	1± 4
24.6.49	0·2 milliunit insulin.	7± 5
1.7.49	0·2 milliunit insulin.	15±7
13.7.49	0·2 milliunit insulin.	38± 9

[1] The result indicates that the plasma insulin content=0.

CASE III.—A.F., a male patient, aged forty-two years, had a blood sugar content at the time of experiment of 376 milligrammes per 100 millilitres. The results obtained with rats of group AB_2 are shown in Table III.

TABLE III.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
16.7.49	0·2 milliunit insulin.	39±8
22.7.49	0·5 millilitre patient's plasma.[1]	3±6
26.7.49	0·2 milliunit insulin.	3±4
4.8.49	0·2 milliunit insulin.	0±2

[1] The results indicate that the plasma insulin content=0.

The animals used in Case III were killed at this stage and a number used for the purpose of checking the insulin effect in isolated muscle according to the technique of Gemmill (1941) (see Table XIX).

CASE IV.—R.J., a male patient, aged twenty-five years, had a blood sugar content at the time of experiment of 256 milligrammes per 100 millilitres. The results obtained with rats of group AB_2 are shown in Table IV.

CASE V.—A.S., a female patient, aged sixty-four years, had a blood sugar content at the time of experiment of 238 milligrammes per 100 millilitres. The results obtained with rats of group AB_1 are shown in Table V.

TABLE IV.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
11.9.49	0·2 milliunit insulin.	41±7
15.9.49	0·5 millilitre patient's plasma.[1]	33±6
19.9.49	0·2 milliunit insulin.	43±6
22.9.49	0·2 milliunit insulin.	42±8

[1] The results indicate that the plasma insulin content=0·28 milliunit per millilitre.

CASE VI.—E.L., a female patient, aged thirty-seven years, had a blood sugar content at the time of experiment of 352 milligrammes per 100 millilitres. The results obtained with rats of group A_2 are shown in Table VI.

TABLE V.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
27.7.49	0·2 milliunit insulin.	45± 6
31.7.49	0·5 millilitre patient's plasma.[1]	2± 1
4.8.49	0·2 milliunit insulin.	0± 2
11.8.49	0·2 milliunit insulin.	2± 4
18.8.49	0·2 milliunit insulin.	2± 6
25.8.49	0·2 milliunit insulin.	5± 4
1.9.49	0·2 milliunit insulin.	16± 9
8.9.49	0·2 milliunit insulin.	43±11

[1] The results indicate that the plasma insulin content=0.

CASE VII.—S.R., a male patient, aged fifty-two years, had a blood sugar content at the time of experiment of 486 milligrammes per 100 millilitres. The results obtained with rats of group A_1 are shown in Table VII.

TABLE VI.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
14.8.49	0·2 milliunit insulin.	42±8
19.8.49	0·5 millilitre patient's plasma.[1]	0±2
23.8.49	0·2 milliunit insulin.	2±3
30.8.49	0·2 milliunit insulin.	1±4
6.9.49	0·2 milliunit insulin.	6±6
13.9.49	0·2 milliunit insulin.	12±6
24.9.49	0·2 milliunit insulin.	39±8

[1] The results indicate that the plasma insulin content=0.

CASE VIII.—B.A., a male patient, aged fifty years, had a blood sugar content at the time of experiment of 427 milligrammes per 100 millilitres. The results obtained with rats of group AB_1 are shown in Table VIII.

TABLE VII.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
14. 9.49	0·2 milliunit insulin.	41± 8
18. 9.49	0·5 millilitre patient's plasma.[1]	2± 2
22. 9.49	0·2 milliunit insulin.	2± 2
29. 9.49	0·2 milliunit insulin.	0± 3
6.10.49	0·2 milliunit insulin.	2± 3
13.10.49	0·2 milliunit insulin.	3± 3
20.10.49	0·2 milliunit insulin.	12± 6
27.10.49	0·2 milliunit insulin.	38±12

[1] The results indicate that the plasma insulin content=0.

CASE IX.—F.B., a female patient, aged forty-seven years, had a blood sugar content at the time of experiment of 324 milligrammes per 100 millilitres. The results obtained with rats of group AB_1 are shown in Table IX.

CASE X.—B.E., a female patient, aged forty-six years, had a blood sugar content at the time of experiment of 403 milligrammes per 100 millilitres. The results obtained with rats of group AB_3 are shown in Table X.

TABLE VIII.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
8.9.49	0·2 milliunit insulin.	43±11
18.9.49	0·5 millilitre patient's plasma.[1]	35± 8
22.9.49	0·2 milliunit insulin.	41± 9
29.9.49	0·2 milliunit insulin.	42± 7

[1] The results indicate that the plasma insulin content=0·32 milliunit per millilitre.

CASE XI.—J.S., a male patient, aged thirty-six years, had a blood sugar content at the time of experiment of 372 milligrammes per 100 millilitres. The results obtained with rats of group A_4 are shown in Table XI.

TABLE IX.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
29. 9.49	0·2 milliunit insulin.	42±7
6.10.49	0·5 millilitre patient's plasma.[1]	3±5
10.10.49	0·2 milliunit insulin.	8±4
17.10.49	0·2 milliunit insulin.	10±6
24.10.49	0·2 milliunit insulin.	38±9

[1] The results indicate that the plasma insulin content=0.

The group used in Case XI was killed and some rats were used to determine the effect of insulin on the isolated diaphragm (see Table XX).

TABLE X.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
22. 9.49	0·2 milliunit insulin.	42± 8
29. 9.49	0·5 millilitre patient's plasma.[1]	34± 9
6.10.49	0·2 milliunit insulin.	44±12
13.10.49	0·2 milliunit insulin.	41± 9

[1] The results indicate that the plasma insulin content=0·30 milliunit per millilitre.

Unselected, Stable Diabetic Patients.

The results obtained with unselected, stable diabetic patients are set out in Tables XII to XV.

TABLE XI.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
2.11.49	0·2 milliunit insulin.	39±7
7.11.49	0·5 millilitre patient's plasma.[1]	0±2
11.11.49	0·2 milliunit insulin.	2±2
18.11.49	0·2 milliunit insulin.	2±1

[1] The results indicate that the plasma insulin content=0.

CASE XII.—E.R., a female patient, aged fifty-eight years, had a blood sugar content at the time of experiment of 90 milligrammes per 100 millilitres; she was receiving 32 units of regular insulin/protamine zinc insulin (R/PZI) mixture daily. The results obtained with rats of group AB_3 are shown in Table XII.

CASE XIII.—J.K., a female patient, aged thirty-seven years, had a blood sugar content at the time of experiment of 160 milligrammes per 100 millilitres; she was receiving 40 units of R/PZI mixture daily. The results obtained with rats of group A_1 are set out in Table XIII.

TABLE XII.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
13.10.49	0·2 milliunit insulin.	43±11
17.10.49	0·5 millilitre patient's plasma.[1]	28± 7
20.10.49	0·2 milliunit insulin.	41± 8
27.10.49	0·2 milliunit insulin.	40±10

[1] The results indicate that the plasma insulin content=0·20 milliunit per millilitre.

CASE XIV.—E.K., a male patient, aged forty-one years, had a blood sugar content at the time of experiment of 151 milligrammes per 100 millilitres; he was receiving 36 units of R/PZI mixture daily. The results obtained with rats of group AB_4 are shown in Table XIV.

TABLE XIII.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
27.10.49	0·2 milliunit insulin.	38±12
31.10.49	0·5 millilitre patient's plasma.[1]	31± 9
4.11.49	0·2 milliunit insulin.	41± 9
11.11.49	0·2 milliunit insulin.	40± 8

[1] The results indicate that the plasma insulin content=0·22 milliunit per millilitre.

CASE XV.—J.B., a male patient, aged thirty-eight years, had a blood sugar content at the time of experiment of 143 milligrammes per 100 millilitres; he was receiving 28 units of R/PZI mixture daily. The results obtained with rats of group AB_4 are shown in Table XV.

TABLE XIV.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
13.10.49	0·2 milliunit insulin.	41± 9
17.10.49	0·5 millilitre patient's plasma.[1]	32± 6
21.10.49	0·2 milliunit insulin.	42±11
28.10.49	0·2 milliunit insulin.	40± 7

[1] The results indicate that the plasma insulin content=0·26 milliunit per millilitre.

Insulin-Resistant Diabetic Patients.

The results obtained with insulin-resistant diabetic patients are set out in Tables XVI and XVII.

TABLE XV.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum.*
28.10.49	0·2 milliunit insulin.	40±7
1.11.49	0·5 millilitre patient's plasma.[1]	32±8
5.11.49	0·2 milliunit insulin.	39±8
12.11.49	0·2 milliunit insulin.	41±9

[1] The results indicate that the plasma insulin content=0·24 milliunit per millilitre.

CASE XVI.—E.W., a female patient, aged fifty-four years, had a blood sugar content at the time of experiment of 406 milligrammes per 100 millilitres; she was receiving 900 units of insulin daily. The results obtained with rats of group 1 are shown in Table XVI.

CASE XVII.—M.McM., a female patient, aged sixty-three years, had a blood sugar content at the time of experiment of 382 milligrammes per 100 millilitres; she was receiving 900 units of insulin daily. The results obtained with rats of group 2 are shown in Table XVII.

TABLE XVI.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum*.
16.4.49	0·2 milliunit insulin.	38 ± 6
20.4.49	0·5 millilitre patient's plasma.[1]	3 ± 3
28.4.49	0·2 milliunit insulin.	2 ± 3
4.5.49	0·2 milliunit insulin.	2 ± 2
10.5.49	0·2 milliunit insulin.	0 ± 3
18.5.49	0·2 milliunit insulin.	21 ± 11
7.6.49	0·2 milliunit insulin.	37 ± 9

[1] The results indicate that the plasma insulin content = 0.

The group used in Case XVII was killed and a number of the animals used for a check on insulin action in the isolated diaphragm (see Table XXI).

TABLE XVII.

Date.	Material Injected.	Fall in Blood Sugar Level in Milligrammes *per Centum*.
7.8.49	0·2 milliunit insulin.	41 ± 9
11.8.49	0·5 millilitre patient's plasma.[1]	2 ± 3
16.8.49	0·2 milliunit insulin.	7 ± 12
19.8.49	0·2 milliunit insulin.	3 ± 6
26.8.49	0·2 milliunit insulin.	3 ± 4

[1] The results indicate that the plasma insulin content = 0.

Results of Gemmill Experiments.

The results of Gemmill experiments are set out in Tables XVIII to XXI.

For Table XVIII (iv) and Table XIX (iv), $n = 9$, $T = 9{\cdot}08$, $P < 0{\cdot}001$.

For Table XVIII (iv) and Table XX (iv), $n = 9$, $T = 10{\cdot}41$, $P < 0{\cdot}001$.

For Table XVIII (iv) and Table XXI (iv), $n = 9$, $T = 10{\cdot}52$, $P < 0{\cdot}001$.

TABLE XVIII.

Results of Gemmill Experiments in a Control Series of A.D.H.A. Animals. (Taken from "Endocrine Influences on Glycogen Deposition in the Isolated Rat's Diaphragm", Bornstein and Trewhella, 1950*b*.)

Glycogen in Grammes per 100 Grammes of Wet Tissue.			
(i) Start.	(ii) Without Insulin.	(iii) With Insulin.	(iv) Difference.
0·29	0·29	0·68	0·39
0·38	0·47	0·89	0·42
0·26	0·28	0·84	0·56
0·31	0·31	0·68	0·37
0·30	0·32	0·72	0·40
0·24	0·26	0·68	0·42
0·28	0·30	0·74	0·44
0·34	0·36	0·79	0·43
Mean .. 0·30	0·32	0·75	0·43

For Table XVIII (iv) and Tables XIX, XX, XXI (iv) (combined), $n = 15$, $T = 17{\cdot}22$, $P < 0{\cdot}001$.

(T is the index of variability of the mean and P the possibility of the experimental results' being due to chance. Therefore there is less than one chance in a thousand that these figures are accidentally produced.)

Discussion.

These experiments show that injection of plasma from patients in Cases I, II, III, V, VI, VII, IX, XI, XVI and XVII into A.D.H.A. rats produced in them in each instance resistance to a normally effective dose of insulin. The duration of the resistance varied, lasting up to six weeks. It is to be noted that in these patients insulin, as assayed by the method of Bornstein (1950*b*), was absent from the plasma.

TABLE XIX.

Results of Gemmill Experiments in a Series of A.D.H.A. Rats Injected with Plasma of Patient A.P. (Case III).

Glycogen in Grammes per 100 Grammes of Wet Tissue.			
(i) Start.	(ii) Without Insulin.	(iii) With Insulin.	(iv) Difference.
0·31	0·33	0·38	0·05
0·44	0·43	0·47	0·04
0·30	0·31	0·44	0·14
Mean .. 0·34	0·36	0·43	0·08

TABLE XX.

Results of Gemmill Experiments in a Series of A.D.H.A. Rats Injected with Plasma of Patient J.S. (Case XI).

Glycogen in Grammes per 100 Grammes of Wet Tissue.			
(i) Start.	(ii) Without Insulin.	(iii) With Insulin.	(iv) Difference.
0·29	0·31	0·39	0·08
0·33	0·35	0·37	0·02
0·31	0·31	0·36	0·05
Mean .. 0·31	0·32	0·37	0·05

Plasma from patients in Cases IV, VIII, X, XII, XIII, XIV and XV, in all of whom detectable insulin was present in the plasma, either normally or as a result of injection of insulin, failed to produce insulin resistance in the animals.

TABLE XXI.

Results of Gemmill Experiments in a Series of A.D.H.A. Rats Injected with Plasma of Patient M.McM. (Case XVII).

Glycogen in Grammes per 100 Grammes of Wet Tissue.			
(i) Start.	(ii) Without Insulin.	(iii) With Insulin.	(iv) Difference.
0·28	0·32	0·41	0·09
0·36	0·37	0·42	0·05
0·32	0·34	0·39	0·05
Mean .. 0·32	0·34	0·40	0·06

With the patients in Cases III, XI and XVII the insulin resistance was confirmed by a Gemmill (1941) experiment, in which the glycogen deposited in the isolated rat's diaphragm may be taken as an indication of insulin activity. If the control series (Table XVIII) is compared with each of the groups previously injected with plasma obtained from diabetic patients in Cases III, XI and XVII

(Tables XIX, XX and XXI), a pronounced diminution in the glycogen deposition is noted, and therefore reduced insulin activity is indicated.

Thus it is shown that the injection of plasma obtained from some diabetics into A.D.H.A. rats is capable of diminishing the action of insulin in the isolated diaphragm.

It has been shown previously (Bornstein and Trewhella, 1950*b*) that plasma from such patients (Cases I, II, VII and IX) has no direct destructive effect on insulin, and so it must be considered that this resistance is due to an action on the tissues of the animal.

The fact that this effect could not be produced by the plasma of diabetic patients who were stable on insulin (Cases XII, XIII, XIV and XV) suggests that whatever the antagonistic factor may be, it is "neutralized" by the administration of excess insulin. It is possible, however, that these patients fall into the same group as those in Cases IV, VIII and X, in whom normal concentrations of insulin were present.

To date we have been unsuccessful in our efforts to identify the nature of this "factor".

The series of patients investigated is not large enough to indicate whether this factor plays a significant role in the majority of diabetic patients.

Summary.

1. The alloxan diabetic, hypophysectomized, adrenalectomized (A.D.H.A.) rat, a preparation extremely sensitive to all substances influencing the blood sugar level, has been used to determine whether plasma obtained from diabetic patients has any effect on the sensitivity to insulin of such preparations.

2. The techniques employed were the insulin assay described by Bornstein (1950*a*) and the glycogen deposition in the isolated rat's diaphragm described by Gemmill (1941).

3. The results show that plasma taken from some diabetic patients, when injected into A.D.H.A. rats, diminished the sensitivity of these preparations to insulin.

4. The common characteristic of all patients whose plasma had this effect was an absence of detectable insulin in the plasma.

5. Plasma containing insulin, either naturally or as a result of insulin administration, did not produce this effect.

6. The significance of this finding is discussed.

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Reviews.

FURTHER RARE DISEASES.

IT can be asserted without fear of contradiction, that if a bird is sitting upon a lamp-post, it is far more likely to be a sparrow than a canary; however, from the subject matter of "Further Rare Diseases and Debatable Subjects", by F. Parkes Weber,[1] it is obvious that the author was ever on the lookout for the odd canary, and herein he has built up a large series of rare maladies to add as a companion volume to his previous publication of a similar name. The rarity of any object or topic is essentially comparative, and what may be rare to a practising physician may border on the commonplace to a research worker; but this book is devoted to such a wide field of subjects that some of its pages will prove intriguing to all medical men. Some of the topics discussed include *carcinoma telangiectaticum*, hæmatospermia, Sjøgren's disease, cerebello-olivary degeneration, and death while bathing, to mention a discursive selection.

As well as the above mentioned there are many other rare entities, which go to make up a most unusual volume and one which will prove interesting reading to all who like to elucidate the medical mysteries that appear from time to time like a *rara avis*.

[1] "Further Rare Diseases and Debatable Subjects", edited by F. Parkes Weber; 1949. London: Staples Press, Limited. New York: Staples Press, Incorporated. 8½" × 5½", pp. 244, with many illustrations. Price: 25s.

MALARIOLOGY.

THE intensive research of recent years into the many aspects of malaria has led to the accumulation of a great volume of information on the subject. This formed the basis for the successful antimalarial work of the tropical campaigns, and is no less valuable in affording an effective approach to the problem in civilian practice. The extent both of the recent literature and of the yet unpublished experience has existed as a serious drawback to work in all fields of malaria. There has consequently been an urgent need for a detailed reference book on the subject. Dr. Mark F. Boyd, with the assistance of sixty-five collaborators, has successfully achieved this ambitious task in the two packed volumes of his "Malariology".[1]

The book was planned as "a working manual of malariology and a comprehensive and adequate review of all available knowledge relating to malaria", and its authors were selected as "recognized authorities throughout the world who have been recently actively engaged on the particular aspects of malaria with which they deal". In general, the authority of the various chapters is ensured by the names of the writers responsible, together with the eminence of Dr. Boyd, both as a worker and as an editor in this field. Among the many well-known authors represented are Sir Rickard Christophers, Emile Brumpt, P. A. Buxton, L. W. Hackett, Sir Gordon Covell, W. H. Taliaferro, S. P. James, Sir Malcolm Watson and F. L. Soper.

The work is divided into five parts, which deal in turn with an historical review, parasitology, the anopheline vectors, the human host, and malaria control and eradication. During the lengthy period necessary for its publication, further important progress has been made in some branches of the subject. For this reason inevitable omissions occur, especially in regard to the recent work on the exo-erythrocytic stages of the human parasites, and specific treatment and insecticides. Apart from such defects arising from the rapid advances in malariology, the 1643 pages of the book cover every aspect of the subject with encyclopædic thoroughness.

Among the sections of mainly local significance, Willard V. King, who is known to Australian malariologists for his war work in the south-west Pacific, contributes a valuable chapter on the Australasian anophelines. This incorporates, with acknowledgements, much information from the monograph of Lee and Woodhill, including their distribution charts. Keys to the adults and larvæ of the species are included. Malaria control in the Australasian region is dealt with by Edward Ford in a chapter which embodies Australian war experience, and takes into account economic and other difficulties. A review of local antimalarial measures fails to mention the important Queensland Government scheme by which municipalities are subsidized for mosquito control work.

In an interesting chapter on malarial incidence in Australia and the south Pacific by S. M. Lambert, the problem of possible wide implantation of malaria in Australia is mentioned. As the author states, the general dispersal of anophelines, associated with returning infected troops, posed a grave problem for health authorities, especially as occasional cases had occurred in southern Australia. However, Australian workers now consider that such risk is limited to tropical parts of the continent, north of 19° south latitude, and within the range of *Anopheles punctulatus farauti*. Except for odd cases and localized outbreaks, particularly in southern Queensland, little danger is feared

[1] "Malariology: A Comprehensive Survey of all Aspects of This Group of Diseases from a Global Standpoint", edited by Mark F. Boyd. Volumes I and II; 1949. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 10" × 7", pp. 1643, with 436 illustrations. Price: £16 12s. 6d. a set.

in areas south of the line mentioned. It cannot be agreed that the time of the first arrival of malaria in Australia can be fixed closely by the reports of Gray and von Mueller, that the disease was not found in northern and north-west Australia during their visits. The intermittent character of its incidence in those parts, and the fact that infected Macassar crews had regularly visited the northern coasts before this time, perhaps for centuries, render such estimate valueless. Nor is the conjecture that malaria was first spread through Melanesia by early Portuguese and Spanish navigators at all convincing. Many experienced readers will also disagree with the author's estimate of the relatively low severity of Melanesian malaria, both in natives and in Europeans.

This important work must prove of the greatest value to all specialists in the subject. It is disappointing that its high local cost will preclude a wider circulation.

RADIOTHERAPEUTIC PRACTICE.

RADIOLOGICAL TECHNICIANS will be grateful for a short textbook of radiotherapeutic practice designed to meet their needs.[1]

The authors devote the first five chapters to fundamental physical considerations and an elementary explanation of the physical foundations of radiotherapy is given. This section is the least satisfactory portion of the book, for the student technician needs a much fuller physical training than is covered within these pages. The physical work is explained in simple terms and should be helpful to the student who has little prior physical knowledge. It is hoped that the demand for this volume will induce the authors to produce a greatly enlarged physical section in future editions.

The major part of the work on radiotherapeutic practice is well presented. It commences with a well-written chapter in which the authors explain simply the nature and modes of tumour growth. However, the explanations of the actions of the radiations on living tissues and the treatment of reactions could be taught more clearly.

The principles underlying the prescription of radiation dosage, treatment planning, calculation and administration are described with commendable clarity. The authors then illustrate these general principles by giving in detail therapeutic techniques applicable to particular major sites. Generally they accomplish their objects to the reader's satisfaction and the numerous diagrams throughout the book enhance the value of the text.

Inter alia, carcinoma of the breast is chosen to illustrate treatment methods, but some unfortunately chosen diagrams are included. The glancing fields shown in Figure 129 do not include sufficient chest wall; in Figure 131 the medial tangent does not include the parasternal skin, and the diagram (Figure 127) of a dreadful breast radium implant should be eliminated.

The duties and responsibilities of technicians are laid down, and safe working procedures are clearly defined for them. The student will be helped by the numerous footnotes which explain etymological derivations of medical terms.

Walter and Miller are commended and thanked for producing this volume which henceforth every radiotherapy technician must regard as an essential possession.

THE HINGE GRAFT OR GINGLYMUS IMPLANT.

PROFESSOR ARNOLD K. HENRY'S brochure on "The Hinge Graft or Ginglymus Implant" presents orthopædic and plastic surgeons with a new approach to some of their problems.[2] Should Professor Henry's results be repeated in a large number of cases, and should those results be maintained over a period of years, then it must be conceded that the "hinge graft" is indeed a valuable contribution to surgery.

This booklet should be studied by all orthopædic and plastic surgeons—especially by the younger members of those specialties. Greater details and pen sketches of the operation described on pages 3 and 5 would clarify the exact location of the grooves cut to receive the grafts and the technique of "suturing the tendons back over the grafts". Professor Henry's "Reflections on Grave Calcanean Fracture" must be treated with caution and reserve, as the ill effects could far outweigh any benefits derived from the procedure advocated.

One is induced to ask why the extremities of the graft on the lateral aspect of Figure 17a are not in intimate contact with the femur and tibia; also in this figure the grafts are shown to be broader than they are thick, and thus the description on page 19 of the grafts being "one-fifth of an inch in diameter" is rather ambiguous. The correct widths and thickness of the grafts are important details to those who may attempt the operation.

Professor Henry's suggestion regarding replacement of enucleated phalanges by the "hinged grafts" is ingenious and appears worthy of trial in suitable cases, whilst his "wishful thoughts on hinge grafts" are commended to plastic surgeons for consideration.

BIOCHEMISTRY.

THE era of Greek heroes still lives for those who, like Cantarow and Trumper, attempt in dual harness the Herculean task of presenting in their fourth edition of "Clinical Biochemistry" a comprehensive survey of so wide a field.[1] The book covers the ground adequately, critically and without bias. It contains a wealth of up-to-date knowledge and can be highly recommended. The title of the book does not do credit to the subject matter, which is more than clinical if that word is used in the sense of "applied". Indeed, the authors lead us into many paths which more than border on fields of research and are not traversed in a well-equipped routine laboratory. The book should prove most useful for reference, as the authors first present the various diseases and the possible biochemical findings arising therefrom and then turn about and relate the biochemical findings to various diseases. This should prove most convenient for those wishing information in either of the two directions.

Perhaps attention should be drawn to a few features which are not pleasing.

Firstly, the section on basal metabolism contains a definition of basal metabolic rate which is incorrect. Thus on page 299 we read "the basal metabolic rate is then expressed in terms of calories per square meter of body surface per hour".

Discussing the basal metabolic rate in hyperthyreoidism, the authors observe, page 303, "values above +100 have been observed, cases showing values of +20 to +50 being considered mild or moderately severe, +50 to +75 severe etc.". The assessment of the degree of severity in these terms would not find support from experienced metabolists. On the whole, this chapter is comparatively weak.

In the chapter on renal diseases, the authors are not critical enough of the limitations of the urea clearance test.

The chapter on chemical investigation of gastric function is in need of rewriting in some parts. The "types of meal" do not include meat extract broths which are so commonly employed.

The section on total chlorides ignores the secretion by the stomach of neutral chlorides as such, and the erroneous idea of neutralization of hydrochloric acid by the regurgitation of duodenal contents is still presented.

In the section on hypoacidity, page 472, we read, "hypoacidity is commonly observed in . . . chronic constipation, chronic appendicitis etc." On the section on hyperacidity, page 476, we find "it is found in cases of chronic appendicitis and chronic constipation". Also in the section on hyperacidity we find "clinical hyperacidity is due to one or more of the following factors: (*a*) Secretion of an abnormally large volume of gastric juice (hypersecretion). (*b*) Failure of the volume of secretion to diminish during the second hour. (*c*) Delayed gastric evacuation." Loose thinking of this nature is out of place in a book of so high a general standard.

The final chapter on hormone assay and endocrine function is written by A. E. Rakoff, and is particularly well done. By an oversight, the authors in their preface do not advise the reader of this welcome addition. Perhaps in future editions, other specialists may be invited to deal with one or other aspect of a science that few can compass and none can master.

[1] "A Short Textbook of Radiotherapy for Technicians and Students, with a Supplementary Chapter for the Dermatologist", by J. Walter, M.A., B.M. (Oxford), M.R.C.P. (London), D.M.R.E. (Cambridge), and H. Miller, M.A., Ph.D. (Cambridge), F.Inst.P., with a foreword by J. L. A. Grout, M.C., F.R.C.S. (Edinburgh), F.F.R., D.M.R.E.; 1950. London: J. and A. Churchill, Limited. 8½" × 6", pp. 456, with 199 illustrations. Price: 28s.

[2] "The Hinge Graft or Ginglymus Implant", by Arnold K. Henry, M.B. (Dublin), M.Ch. (Hon. Cairo), F.R.C.S.I.; 1950. Edinburgh: E. and S. Livingstone, Limited. 9½" × 7", pp. 72, with 47 illustrations. Price: 15s.

[1] "Clinical Biochemistry", by Abraham Cantarow, M.D., and Max Trumper, Ph.D.; Fourth Edition; 1949. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical) Proprietary, Limited. 9" × 6¼", pp. 668, with 38 illustrations. Price: £3 16s.

The Medical Journal of Australia

SATURDAY, JANUARY 20, 1951.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE HOSPITAL ALMONER PROBLEM.

THERE is a hospital almoner problem. It is not a problem of what work hospital almoners shall do, of how they shall be trained to do their work, or of the value of their work when it is efficiently done. These things are known and realized, though there may be some difference of opinion in some details. Apparently the difficulty lies in the finding of women suitable and willing to be trained for the work, and having been trained, willing to do it. Advice has been received that the Council of the New South Wales Institute of Hospital Almoners is much concerned on the one hand with the increasing demand for almoners in hospitals, and on the other with the falling off in the number of applicants for training. The reason for this should be sought and if possible some remedy found.

Though the first hospital almoner in England was appointed at the Royal Free Hospital in London in 1895, it was not until 1929 that an Institute of Hospital Almoners was formed in Victoria. An Institute of Almoners was formed in New South Wales about eight years later. Since then the importance of the work of almoners has been widely recognized in Australia and it may be taken as true that no large modern hospital is complete unless it has an almoner service. For example, word has recently been received that at a mission hospital for children started a year or two ago at Singapore an almoner has been appointed. About 115 almoners are already working in Australia. For those who do not know the full extent of an almoner's duties a statement set out in these columns in 1937 may be reproduced:

1. To ensure as far as possible that poverty, home difficulties or lack of understanding shall not prevent patients from receiving the full benefit of treatment prescribed.

2. To act as a link between the hospital and outside agencies, State or voluntary.

3. To acquire a knowledge of the patient's circumstances and home conditions, by visiting and detailed inquiry, for the use of the medical staff.

4. To organize the after-care of the patient on discharge.

5. If required to do so, to check abuse of the hospital by patients (*a*) who are in a position to pay for private treatment, (*b*) who do not require special hospital treatment, and (*c*) who can arrange for home treatment.

6. If required to do so, to assess and collect patients' contributions towards treatment and maintenance in hospital.

Under these headings are included arrangements for supplying correct surgical appliances and for planning convalescence or holidays; for providing special diets; for raising financial assistance for patients in cooperation with outside agencies; for finding accommodation for country patients and destitute men and women attending in the out-patient department; for transport to and from the hospital; for institutional care and home treatment to free hospital beds for more urgent cases; for the constant watching and visiting of patients to prevent relapse and further hospital treatment, *et cetera*.

From this statement it is clear that much of the almoner's work can be classified as belonging to the sphere of preventive medicine; moreover, in the curative sphere it does a good deal to convert out-patient treatment into a partial domiciliary service. It will also be clear that, in these days when hospital beds are in great demand and patients are discharged to their homes after an unusually, and sometimes an incredibly, short stay in hospital, the safety factor is strengthened, and in no small degree.

It has been stated that the New South Wales Institute of Hospital Almoners is worried about the shortage of trainees. What should be an increasing number is fast diminishing; when the figures are considered at the same time as the growth in the population and, with it, the increase in the demand, and the need, for hospital treatment, they become the more clamant. The number of almoners who have been trained in the last few years by the New South Wales Institute is as follows: in 1947, 16; in 1948, 14; in 1949, 10; in 1950, 7. If the present trend continues, New South Wales will soon be recruiting no fresh almoners. At least sixteen posts are waiting to be filled.

Let us look at the type of training undergone in preparation for the almoner's work—we quote from a circular issued by the Australian Association of Almoners (Miss M. Bowman, Honorary Secretary, Almoner Department, The Alfred Hospital, Melbourne). The course of training includes study of the social sciences and social work, some aspects of public health and hospital administration, and the social implications of disease. Supervised practical work is carried out in a variety of social agencies and hospitals. Several courses are available in Australia. The University of Melbourne offers a course of three years' duration, leading to a diploma in social work; medical social work is taken in the third year of the course. A degree in arts or commerce may be obtained in combination with the diploma in four years. The Universities of Sydney and Adelaide offer courses of two years' duration leading to a diploma in social work. Holders of the diploma must then complete a third year of study in medical social work; this may be undertaken either in the University of Melbourne or with the New South Wales Institute of Hospital Almoners. The minimum age for the beginning of training is nineteen years in Melbourne and twenty in Sydney and Adelaide. The fees vary in the different centres—from £25 to £45 for the first and second years and from £15 15s. to £35 10s. for the third year. In certain circumstances grants and

scholarships to cover fees and living expenses are available. It will be clear that successful training demands intelligence and a close application to study. According to the Australian Association of Almoners the trainee should have patience, tolerance, thoughtfulness, sound judgement, imagination and a sense of humour. From the nature of the work it is clear that an almoner should have a feeling of vocation. She should like the work for its own sake—because she wishes to do something to help her fellow man. Most people will think that the number of women in the community who are actuated by ideals of service is not less than it was in the past. It may be that the idea of provision by the State of help for people in many aspects of their lives is obscuring the need for sympathetic help by persons of understanding. The practitioners of medicine are among those who can dispel these notions. In any case, whether ideals of service abound or not, the service, when it is given, should be properly remunerated. An almoner after three years of training receives a salary "in the vicinity of £350 to £400" *per annum*—an amount which does not appear sufficient in comparison with what is paid to workers in factories and offices. It is essential that payment must be on a higher rate than it is at present and there is no hope for the Australian almoner services unless this is done. But it is also true that payment is not the only consideration.

Current Comment.

MEASURES TO LESSEN THE HAZARDS OF BOXING.

EVERY little while a public outcry arises over a major catastrophe associated with boxing. Less attention is paid to the minor hazards of the sport, although most doctors and some of the general public are aware of them. The problem is, of course, to decide what of a practical nature can be done about it. In this, certain steps taken recently in the United States provide food for thought. Two years ago the Medical Advisory Board of the New York State Athletic Commission was created by State law with a membership of nine. This board has recently announced[1] a new set of medical rules and regulations for boxers and wrestlers who participate under its jurisdiction. A comprehensive initial medical examination is to be required before boxers and wrestlers are licensed. An examination will also be mandatory with the renewal of the licence each year. All contestants will be given an examination at the noon weighing-in on the day of the contest and another just before the bout; for championship or important matches a further special examination five days before the contest will be required. Injuries or illness suffered during training for a match must be reported and followed up with appropriate medical appraisal and recommendations. When any question arises of the physical ability of a contestant to participate safely, a panel of doctors designated by the Medical Advisory Board will make the final decision. During bouts the ringside attending doctor may enter the ring between rounds to evaluate the apparent or latent injury. When in his judgement the contestant is in danger of serious injury, he shall advise the referee that the contest be terminated. After a knockout or severe injury the ringside doctor will render emergency care and make recommendations for further treatment. He may require that the participants remain in the arena long enough for necessary emergency care, observation and advice. Any contestant with a severe injury not requiring admission to hospital must be reexamined within twenty-four hours. The regulations also contain special stipulations to be invoked after a series of losses or after severe injury or knockout to prevent cumulative injury. Methods of reporting the results of examination, the record of injuries and their treatment, and, in fact, the complete participation record of the athlete are designed, it is stated, to provide the commission with the essential tools for determining within human limitations the fitness of contestants to take part in boxing and wrestling contests with the greatest possible degree of safety. This is a reasonable aim which should commend itself generally.

Another action recently taken may arouse more controversy. It is reported[1] that the Joint Committee on Health Problems in Education of the National Educational Association and the American Medical Association has passed a resolution disapproving boxing as an interschool activity. The committee, it is stated, based its action primarily on the premise that boxing is one of the few sports in which the offensive goal is to strike the opponent and in which the head is a principal target; there is a resultant potential of permanent injury to the central nervous system, particularly the brain, that may bring about a loss of mental power and physical coordination. Realizing that boxing will be continued, the committee has also outlined exacting health and safety precautions to be taken in that event; but the feeling is that few schools can provide the essential equipment and facilities, the trained teaching staff and the medical supervision needed to ensure optimum conditions of safety. No doubt these views will be assailed as likely to develop "softness", but the reasons given are sound. Professional or amateur contests arranged outside a school or similar body are in a different category. It is pointed out that the contestant is usually more mature and participates quite voluntarily; the "stimulus furnished by the sanction and implied approval of an educational institution" leaves little room for choice. The possibility of permanent injury to the brain, of greater or less degree, is very real, as every medically trained person knows.

[1] *The Journal of the American Medical Association*, April 22, 1950, page 1304.

HOMOLOGOUS SERUM HEPATITIS.

HOMOLOGOUS SERUM HEPATITIS, although a generally recognized entity, continues to baffle both those who seek to understand its nature and mode of transmission and those concerned with prevention of the serious and fatal complication it brings to the administration of blood and blood components. Its origin is obscure. Present evidence does not show whether it is or is not a variant of the so-called infectious viral hepatitis; though its transmission seems to take place exclusively through injected human blood products or a blood-contaminated instrument, it is safe to say, as J. R. Paul and H. T. Gardner[2] have drily remarked, that the virus of serum hepatitis did not originate in a syringe. Infectious hepatitis can be spread artificially in the same way as serum hepatitis, but not usually and certainly not exclusively in that way. It is suggested that the virus of serum hepatitis may persist in a symbiotic relationship with its host more readily than the virus of infectious hepatitis, judging by the apparent ability of the virus of serum hepatitis to maintain itself as a viræmia in the blood-stream for long periods of time without causing obvious illness. This characteristic, of course, makes control of serum hepatitis much harder; and although some of the most striking recorded outbreaks have been apparently due to contaminated syringes used in mass inoculations, the most worrying aspect relates to the use of pooled human serum. This problem does not appear to be as great in Australia as in the United Kingdom and in the United States of America, but evidence presented separately by R. J. Walsh, Ian Wood and M. J. J. O'Reilly, at the Australasian Medical

[1] *Ibidem*, page 1298.
[2] *The American Journal of Medicine*, May, 1950.

Congress (British Medical Association) in May-June, 1950,[1] indicates the existence of homologous serum hepatitis in at least three States of Australia. Walsh, in the paper with which the discussion opened, suggested that the incidence might be reduced by cautious use of serum, by preparing serum from small donor pools or by fractionating pools; the virus might be destroyed in serum by ultra-violet irradiation or by chemical sterilization with purified nitrogen mustard. Various writers have laid particular stress on the value of ultra-violet irradiation for destruction of the virus, despite some unsatisfactory results in the early days of its use; but recent reports are not reassuring. Some time ago John R. Neefe,[2] in a progress report on viral hepatitis, pointed out that only one strain of hepatitis virus had been tested for response to ultra-violet irradiation and that not a highly potent strain. He stressed the need for additional confirmatory studies before irradiated plasma could be accepted as free from the risk of viable hepatitis virus. The reality of the risk may be judged from the simultaneous publication[3] of three separate reports of hepatitis (apparently homologous serum hepatitis) following the administration of irradiated human plasma. N. Rosenthal, F. A. Bassen and S. R. Michael were studying the effect of large and frequent phlebotomies followed by plasma infusions in cases of *polycythæmia vera*. Only plasma which had been subjected to ultra-violet irradiation was used. Of 13 patients treated, two became jaundiced between three and four months after receiving the plasma; in a third case a hospital patient developed jaundice seventy-one days after he received plasma from a polycythæmic patient who had received plasma but had shown no sign of viral hepatitis. The evidence indicates that the treated plasma was responsible. In the second paper, R. N. Barnett, R. A. Fox and J. G. Snavely report three cases of severe hepatitis, two of them fatal, developing fifty-six, forty-five and forty-three days after the administration of commercially irradiated plasma. There appears to be no other reasonable source for the virus than the plasma. The third group of cases, discussed in a preliminary report by G. James, R. F. Korns and A. W. Wright, was larger. Of 22 patients who received irradiated plasma, 14 developed apparent homologous serum hepatitis. In the majority of cases the serum was from one particular batch, but when this preliminary report was written, time had been insufficient to allow a full investigation of the procedure for preparing the plasma; so far no apparent irregularities had been noted. The evidence involving the plasma appeared to be strong, as in the other two reports. However, it would be unwise to take alarm and to regard irradiation as discredited. It may yet be found to be unsatisfactory, and other methods of dealing with the problem should by all means be developed. On the other hand there may be other factors, not at the moment obvious, which are responsible for the unhappy results reported. The very considerable success obtained, as against these reports, suggests that the fault may lie in details of technique and not in the basic method.

INTRACTABLE PEPTIC ULCER.

To speak of a lesion like a gastric, duodenal or peptic ulcer as intractable seems like giving up hope, but without our giving way to pessimism on the part of the medical attendant or the often very difficult patient, there is no doubt that sometimes the problem of the relief of recurring pain can extend the ability of therapists from the psychiatrist to the most radical surgeon. Walter L. Palmer, Joseph B. Kirsner and Irwin Levine have used several case histories to illustrate the difficulties of treatment of this common disease or group of diseases.[4] One provocative heading tells one side of the story: "Intractable patients or intractable ulcer?". In this instance the man concerned was a rugged but suggestible person who had never established satisfactory relations with any doctor; happily for a time at least he regained the inner calm previously gained by various measures, including vagotomy, merely by adequate reassurance. At the opposite pole were patients who persistently had recurrences of pain and discomfort even after surgical treatment, sometimes associated with bleeding. The authors remark that whatever the individual circumstances, such patients have an apparently intractable lesion either because of an inability to effect neutralization or inhibition of acid gastric secretion, or because of a complication such as stenosis. They state their experience that, although hypersecretion is not a feature of gastric ulcer as it is of the duodenal variety, acid gastric juice can always be demonstrated over a period of time if a sufficient number of histamine tests are performed. In addition, in gastric ulcer the danger of carcinoma is always present, and partial gastrectomy may solve the potential problems if carried out at an early stage. In patients who have responded to less drastic measures recurrence may take place at variable periods later in association with a returned or increased acid secretion. The authors have found that some such patients may have more or less intractable symptoms. In duodenal ulcer, on the other hand, hypersecretion and stenosis lie at the bottom of intractability, and nocturnal fasting secretion is as a rule greatly increased. For this reason control of the acid secretion is difficult. The authors have had occasional dramatic successes with irradiation of the region of the fundus of the stomach, of course administered with the greatest caution. The term intractability may be applied to some of these cases, because of the possible occurrence of jejunal ulcer, which, as Palmer and his associates state, is, in a sense, of itself intractable. Vagotomy they have found to be the best procedure yet devised. Reviewing the position, the authors conclude that if all medical management fails, in addition to vagotomy, combined perhaps in duodenal ulcer with posterior gastro-enterostomy, gastric resection should be advised, and even further gastric resection, for, as they fatefully remark, ulcers do not recur after total gastrectomy.

In the same issue of his journal Paul A. Binter and Thomas J. Rankin publish the results of a study of the use of tetra-ethyl ammonium chloride for the relief of pain in peptic ulcer.[1] This drug really is, when successfully used, a temporary means of performing pharmacological vagotomy, as it blocks transmission of nerve impulses through the autonomic ganglia. These authors have used the drug in the treatment of 40 out of 70 patients with peptic ulcer, choosing those who had symptoms resistant to other forms of medical therapy. The patients specially studied were 27, whose outstanding complaint was severe pain. Tetra-ethyl ammonium chloride was administered in doses of 500 milligrammes by the intravenous route. It was given once or twice daily according to indications, and was continued for variable periods. As a rule relief from pain was complete within five or ten minutes after administration, and repeated use did not lessen its value. This feature was particularly noted in a few patients who were so treated before undergoing operation. The authors are particularly interested in the mechanism of action of the drug. They do not think it likely that the relief of pain, which is very prompt, is due to a rapid lowering of acid secretion or a duodenal reflux. They prefer the hypothesis that the drug effects blockage of the vagus, bringing about a lowering of gastric motility, thus relieving spasm and preventing distension proximal to the area of partial obstruction due to spasm. Whether this is the correct explanation or not, the results were good, and Binter and Rankin suggest further studies of the method, which might be more used while the patient is under treatment in hospital.

This last series differs from the cases quoted in the article of Palmer and others, but both can be taken to illustrate the point that even experienced gastroenterologists have their difficulties, and that sound judgement, applied in supervision and treatment over perhaps many years, is needed in order to do the best for the person known as "the ulcer patient".

[1] THE MEDICAL JOURNAL OF AUSTRALIA, July 29, 1950, page 183.
[2] *Annals of Internal Medicine*, November, 1949.
[3] *The Journal of the American Medical Association*, September 16, 1950.
[4] *Annals of Internal Medicine*, September, 1950.

[1] *Ibidem.*

Abstracts from Medical Literature.

PATHOLOGY.

Sclerosing Lipogranuloma.

HANS F. SMETANA AND WILLIAM BERNHARD (*Archives of Pathology*, September, 1950) state that sclerosing lipogranuloma is a reactive process which sometimes follows injury to subcutaneous fat tissue. The injury of the adipose tissue may be of varying character and probably sets off the reaction only by interfering temporarily with the local blood supply and fat metabolism. Physical disruption and hæmorrhage are not necessary to the development of sclerosing lipogranuloma. The assumption that formation of fatty acids is essential in the genesis of lipogranuloma is probably erroneous. The character of the reaction does not suggest the presence of such highly irritating substances; moreover, the type of reaction following the introduction of liquid petrolatum and vegetable oils is identical with that seen in "traumatic" lipogranuloma, although the body probably does not possess lipases for these exogenous substances. Spontaneous healing of lipogranuloma is extremely slow, since the only effective means of disposal of fats altered by injury are phagocytosis and transportation or the walling off and segregating of the affected from unaffected areas. Local tissue reaction of this type suggests a profound change in the constitution of fats, brought about in consequence of injury, rendering them unsuitable for further metabolic use. Sclerosing lipogranuloma represents a specific reaction to an unspecific injury and follows a distinct course, which differs from that of the reaction following injury to other tissues. The effects produced by sclerosing lipogranuloma on the body as a whole depend on the location of the process and the possibility that the function of structures situated in the affected areas may be interfered with. The only treatment known to influence the course of sclerosing lipogranuloma is the complete surgical removal of the involved tissues. "Traumatic" sclerosing lipogranuloma is related to, but may be distinguished from, traumatic fat necrosis of the breast, relapsing nonsuppurative nodular panniculitis, *adiponecrosis neonatorum*, lipid pneumonia, pelvic lipogranuloma caused by iodized oils injected for uterosalpingography, and other artificial lipogranulomata.

Neurilemmoblastosis.

KEITH INGLIS (*The American Journal of Pathology*, July, 1950) submits the hypothesis that there is a common factor underlying all the extracerebral lesions comprised in the tuberous sclerosis complex. It is suggested that this common factor is intrinsic in nature and neural in origin, and to it the same neural intrinsic factor is applied. Cellular tissue in renal tumours associated with tuberous sclerosis, as well as cellular tissue found in cystic disease of the lung, widely regarded as involuntary muscle, is interpreted as being akin to specific nerve sheath tissue (neurilemma, sheath of Schwann) and as constituting part of a systemic disease for which the name neurilemmoblastosis is used. Congenital polycystic disease of the kidneys, cystic disease of the lung, and certain developmental abnormalities of the circulatory system are thought to link up with neurilemmoblastosis, possibly at the basic intrinsic factor level.

Primary Diffuse Tumours of the Meninges.

BOYD K. BLACK AND JAMES W. KERNOHAN (*Cancer*, September, 1950) report four cases of diffuse meningeal meningiomatosis. They state that evidence supports the view that there are two types of cells in the meninges. In two of the cases, tumours appear to have arisen from meningothelial cells, one from fibroblasts, and one of mixed type from both meningothelial cells and fibroblasts. This suggests that both elements of the meninges may undergo diffuse neoplasia. The cases were in children or young adults, as have been most cases reported in the literature.

Nonchromaffin Paraganglioma.

RAFFAELE LATTES (*Cancer*, July, 1950) reports four cases of tumours of the carotid-body type arising in unusual locations. In one of these, the tumour originated in the vagus nerve in the region of the *ganglion nodosum*; in the second case, there was a similar involvement of the vagus nerve, associated with a tumour of the carotid body on the opposite side; the tumour in the third patient was essentially intrathoracic, originating in the upper part of the mediastinum and extending into the right supraclavicular space; in the fourth and last case, there were three independent tumours, involving respectively the *ganglion nodosum*, the carotid body and the adventitia of the aortic arch. These tumours are histologically similar to, if not identical with, those arising at the bifurcation of the common carotid artery and with the more recently identified neoplasms originating in the vicinity of the middle ear (glomus-jugulare tumour). Similar to these, they consist of nests and cords of "epithelioid cells" containing no chromaffin granules and placed in a highly vascular stroma. The cases already known in which tumours of this type have a definite multicentric origin, arising more or less simultaneously in the sites where the various carotid-body-like structures can be found normally, seem further to confirm the opinion already expressed elsewhere, namely, that all these structures are actually parts of a system of chemoreceptors, and that in certain conditions the same unknown factor that produces a neoplastic change in one of them can bring about the same change in the others. To the author's knowledge, this is the first report of the occurrence of tumours of the aortic bodies in man.

A Histologic Study of Muscles and Nerves in Poliomyelitis.

JOHN DENST AND KARL T. NEUBUERGER (*The American Journal of Pathology*, September, 1950) have made a histological examination of voluntary muscles and peripheral nerves in 14 fatal cases of acute and chronic poliomyelitis. The muscular changes consisted of early fatty metamorphosis, followed by varying degrees of degeneration, atrophy and late fibrosis. Plasmodial formations of sarcolemmal nuclei were seen frequently in connexion with disintegration of muscle fibres. Hypertrophic fibres were found in late cases. Proof of true regeneration was lacking. The histological picture, as a rule, resembled that of the neurogenic forms of muscular atrophy, but occasionally was reminiscent of that of progressive muscular dystrophy. The nerves showed very early stripe-shaped demyelination and relatively minor change in the axis cylinders. The lesions in the nerves appeared less severe and less extensive than those in the muscles. The pathologic process appeared to be different from Wallerian degeneration. The possibility of direct action of the virus on muscles and nerves must be considered.

Fat Embolism in Trauma.

J. P. WYATT AND P. KHOO (*American Journal of Clinical Pathology*, July, 1950) have studied a consecutive series of 30 subjects who died after trauma, to determine the frequency and amount of intravascular fat embolism. In every instance evidence of intravascular pulmonary fat was present. A similar study in patients who died suddenly from non-traumatic causes or from lingering illnesses did not show notable amounts of intravascular fat.

Localization of Myocardial Infarcts in Heart Muscle Bundles.

WILLIAM B. WARTMAN AND JOHN C. SOUDERS (*Archives of Pathology*, September, 1950) state that the 72 ventricular infarcts discovered in 50 hearts all showed definite patterns which were similar to the known patterns of the cardiac muscle bundles. In some instances the infarct was limited to a single muscle bundle, whereas in others it involved two, three or even all four bundles. The infarct usually involved only a part of a muscle bundle; for example, the posterior sector of both deep muscles was commonly necrotic, but not the entire circumference of either of these muscles. Twenty-five infarcts in 21 hearts were each confined to a single ventricular muscle bundle. Superficial muscle bundles were involved, either alone or in combination with a deep muscle, in 74% of the infarcts. The internal portion of the superficial muscles was involved three times as commonly as the external portion. Deep muscle bundles were involved, either alone or in combination with a superficial muscle, in 51% of cases. The deep sinospiral muscle was affected significantly less frequently than any other muscle. Atrial infarcts were discovered in 21 of the hearts, but always in association with ventricular infarcts. The majority were recent and in the right atrium, which suggests that they may have been a contributory cause of death. The importance of the thickness of the infarct, especially in the left ventricle, is discussed and three types are described: (i) full thickness infarcts; (ii) massive but not full thickness infarcts; and (iii) laminar infarcts. Full thickness and massive but not full thickness infarcts were composed of two or more muscle bundles at the base of the heart, but of only one or at the most two at the apex. Laminar infarcts usually involved one and never more than two bundles. Rupture, aneurysm and thrombosis were related at least

in part to the thickness of the infarct. Both rupture and aneurysm occurred at the apex of the left ventricle after infarction of the superficial muscle bundles, but at the base and mid-portion of the left ventricle only after infarction of the deep muscles. The incidence of rupture was 8%, and it occurred only in new full thickness infarcts. Aneurysm was more common with full thickness and massive infarcts than with laminar infarcts. Mural thrombosis occurred frequently in association with ventricular aneurysm, full thickness infarct and infarction of the subendocardial portion of the superficial muscle bundles. Multiple muscles were involved much more frequently than a single muscle, suggesting that an infarct affecting more than one muscle has a worse prognosis than one affecting a single muscle. No evidence was found to indicate that the prognosis of a myocardial infarct was worse if deep rather than when superficial muscle bundles were involved.

Pancreatic Lesions Associated with Chronic Ulcerative Colitis.

W. PHILIP BALL, ARCHIE H. BAGGENSTOSS AND J. ARNOLD BARGEN (*Archives of Pathology*, September, 1950) state that interstitial pancreatitis was found at necropsy in 46 of 86 consecutive cases of active chronic ulcerative colitis. In two cases the interstitial pancreatitis was acute; in five it was severe and chronic; in 17 it was moderate and chronic; in 22 it was mild and chronic. In addition to these 46 cases there were 11 cases in which definite pancreatic fibrosis and acinar atrophy were present. The pancreatic fibrosis probably represented the healed stage of chronic interstitial pancreatitis. Pancreatic acinar dilatation occurred in 46 cases. The rates of association of these lesions are far in excess of those in the control group. The factors responsible for the pancreatic lesions could not be determined from this study. It is pointed out that the interstitial pancreatitis seen in these cases of colitis differs significantly from the clinico-pathological entities of pancreatic necrosis and chronic relapsing pancreatitis. It is shown that fatty replacement of liver commonly accompanied pancreatic disease in the cases of colitis. No clinical signs of pancreatic disease in the course of ulcerative colitis could be recognized, but it is suggested that appropriate clinical and physiological research in the future may elucidate the significance of these pathological observations.

MORPHOLOGY.

Partial Absence of Radius.

F. G. EVANS *et alii* (*The Anatomical Record*, January, 1950) describe a case of congenital bilateral partial absence of the radius, with the associated hand deformity, in a Mexican girl. They state that the great majority of previously reported cases of congenital radial defects, complete or partial, have been found in individuals of European stock. Congenital absence of the radius is more frequent in males than in females, and complete absence of the bone is more common than partial absence. The carpal and other hand bones most frequently absent in cases of congenital radial defects are the greater multangular, the navicular, the first metacarpal and the phalanges of the thumb. Bilateral partial absence of the radius occurs in 3·1% of the reported cases of congenital radial defects. Congenital radial defects are frequently associated with other anomalies so severe that the individual does not survive long, 60% of the reported cases occurring in fœtuses, newborn babies or infants less than one year of age. Many congenital radial defects are hereditary.

Positions of Mental Foramina.

H. G. TEBO AND I. R. TELFORD (*The Anatomical Record*, May, 1950) report that the usually accepted description (between the apices of the lower bicuspid teeth) of the relative position of the mental foramina to the lower teeth held in only 20·7% to 25·3% of mandibles studied. They found that the most common position of the foramen was at the apex of the lower second bicuspid (46·0% to 52·8%). This is in agreement with the statement in "Gray's Anatomy". A remarkable bilateral symmetry was demonstrated between the sides of the mandibles studied. The mental foramen was found to lie approximately one-fourth of the distance from the *symphysis menti* to the posterior border of the ramus. This relationship is suggested as a more convenient method of locating the foramen in clinical practice.

The Inguinal Canal.

S. B. CHANDLER (*The Anatomical Record*, May, 1950) submits his third report on his studies of the inguinal region. He states that the inguinal canal results from the formation of the *processus vaginalis* in fœtal life. In the adult the canal is oblique, because growth of the body wall shifts the internal ring laterally. An indirect inguinal hernia is the enlargement of a protrusion of the peritoneum into the internal abdominal ring. A hernial protrusion may not contain anything. It may be large enough to hold a large part of the small and large bowel. The gubernaculum is apparently mucoid connective tissue. It probably does does not extend the *processus vaginalis* or exert traction on the testis.

Compensatory Hypertrophy of Peduncle and Pyramid.

W. J. C. VERHAART (*Journal of Comparative Neurology*, February, 1950) describes hypertrophy of the cerebral peduncle and pyramid as the result of destruction of the contralateral corticofugal fibre tracts in early childhood. This is not due to an increase in the number of fibres, but a larger number of thin fibres develop into thicker ones than normally. Developing more thick fibres out of thin ones is a comprehensible way of hypertrophy because, normally, thick fibres develop only after birth.

Basement Membrane.

I. GERSH AND H. R. CATCHPOLE (*The American Journal of Anatomy*, November, 1949) describe the structures "basement membrane" and "ground substance" and define their chemical and physical properties in normal and pathological structures by histochemical procedures. In skin, the basement membrane becomes more prominent and the ground substance less extractable with increasing age. Inflammation leads to disappearance of the basement membrane, followed by reformation. The basement membrane of the thyreoid follicle also becomes more prominent with age and also after hypophysectomy. In developing human placental villi, the ground substance increases in amount. In the developing kidney, there is a continual remodelling of the basement membrane. Basement membranes in the vicinity of rapidly growing transplantable tumours are largely absent, and both these and the ground substance become water-soluble. Comparable changes occur with scurvy and with pulmonary œdema. Ground substance and basement membranes contain glycoproteins whose state of polymerization is thought to be responsible for their outstanding properties and plasticity, including the changes that occur in them. These changes are brought about by enzymes of the mucinase class (hyaluronidase, collagenase). Collagenase activity was identified in many tumours. Depolymerized, water-soluble ground substance stains selectively with the intravital dye Evans blue. This alteration in the state of polymerization is believed to be important in change in permeability of blood vessels, in growth of neoplasms and spread of metastases, and in morphological rearrangements in certain endocrine glands, cartilage and bone. Morphological evidence was obtained to show that connective tissue cells are active in several of the above reactions and may be responsible for secretion of ground substance and of enzymes that modify the ground substance.

Meckel's Cave and Cranial Nerves and Cavernous Sinus.

L. SCHWADRON AND B. C. MOFFETT (*The Anatomical Record*, February, 1950) draw attention to the fact that, although physicians and surgeons have long realized the importance of the cavernous sinus, the anatomical relations of the cranial nerves to it and of the Gasserian ganglion to Meckel's cave are not well illustrated in the literature and the anatomist has trouble in presenting a clear conception of the relations. They find that Meckel's cave, an evagination of the meningeal dura, encloses the motor and sensory roots, most of the trigeminal ganglion and the greater portion of the mandibular nerve. The maxillary and ophthalmic divisions join the ganglion anterior to the cave. The cavernous sinus is related to the oculomotor, trochlear and abducens nerves and to the ophthalmic and maxillary divisions of the trigeminal nerve, but does not extend inferiorly to the mandibular nerve.

Specificity of Epithelium.

R. E. BILLINGHAM AND P. B. MEDAWAR (*Journal of Anatomy*, January, 1950) demonstrate that epithelium retains its specificity of histological type in a physiologically and anatomically foreign environment. They describe operations in which corneal epithelium is transplanted to body skin and *vice versa*. When corneal epithelium is transplanted to the skin, it is invaded and replaced by skin epithelium and *vice versa*.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at Broughton Hall Psychiatric Clinic, Leichhardt, New South Wales, on December 7, 1950. The meeting took the form of a series of clinical demonstrations by the medical superintendent, Dr. Guy Lawrance, and members of the staff of the clinic. Parts of this report appeared in the issues of December 23, 1950, and January 13, 1951.

Anxiety State.

A series of patients were presented with various anxiety states. The first, a married woman, aged thirty-eight years, had been admitted to the clinic in August, 1950, complaining that she was depressed and tearful. She said that six weeks previously she had become very anxious and had been upset by the slightest thing; she could not relax and was tense all the time. She complained of a hot nerve pain on top of her head and a cold feeling at the back of the head and neck, which went across her back. She had a stabbing pain through the left breast, and this went right through into her back. She had no children, and her husband had told her that it was because she was too dry and did not have proper orgasms. She had electric treatment for her stomach muscles and achieved orgasm once after that and again after another electric treatment. She had plenty of sensation, but she was not satisfied unless she produced a full flow of mucus, which she could rarely do. She had been nine years before achieving orgasm, and at present she was in a state of anxiety lest she would not keep on in that happy state. Investigation of her background showed that her home life had been happy and that she had been a hard working useful woman who married at the age of twenty-nine years a man fourteen years her senior; he regarded himself as being too old to want children and by various means (particularly the use of the "safe period") had avoided them, blaming his wife for her barrenness in that she "always remained dry". She was very fond of children. She saw her child-bearing period passing rapidly away, and she had developed an acute anxiety state which had some hysterical features as seen in the pains in the head and chest, the cold sensations *et cetera*. It was pointed out that the illness had developed at the time it did because her emotional life had been disturbed by the sudden death of her brother and her father-in-law about a year previously. In her history was a story of incestuous relations with her brother and intercourse with several boys and with her husband for nine years before marriage; that was when he learnt the method of the safe period. Treatment in such cases was best carried out with a series of psychotherapeutic talks in which the whole situation was reviewed. Patients did not like the first talk or so, but they soon came to regard them as being very helpful and they cooperated fully. In cases in which good insight was opened up the prospects of full recovery were excellent. The patient under discussion had sexual frustration set up by the non-fulfilment of an instinct which had been aroused. She feared that the childlessness was her own bodily fault, whereas she had really been deceived by her partner for years. The husband was a diabetic and a heavy drinker, and her landlady was an unpleasant nagging woman, who caused a good deal of trouble. Physically the patient was fairly well. Her blood pressure was a little high. Her menses were becoming somewhat scanty. She had had electroconvulsive therapy and a course of short psychotherapeutic talks. She had a very fair insight into her state.

A second patient, a married woman, aged thirty-six years, had been admitted to the clinic in February, 1950, because of great anxiety, with symptoms directing attention to her heart. She looked anxious and distressed, and complained of palpitation of her heart, with pain in the sternal area and sighing respirations. She was depressed, and cried during her interview, when she gave a reasonable story. She felt tensed up and unable to concentrate for long periods, and said that she considered her illness to be caused by headaches of a severe nature, set up by her husband's attitude towards her. She expressed a fear of being alone, and said that at times she felt desperate and inclined to end it all. There had been no intercourse for some months, and very little for years, owing to her husband's indifference. She had been nervy and afraid since the birth of her third child eight years before; she had blackouts then, which still occurred in a much lighter form. She had tremors at times, and they became worse when she thought of her illness; that made her unable to do all those things for others which she had always done, because she had always served others and felt inferior to them. The background was that she was the second of three children; she had a younger sister and an elder brother. Her father was always sick (he died of cancer at the age of forty-seven years), and the mother ran a business. They were kind enough to her, but she was never shown any affection such as was craved for by a young child; the parents were always too busy, and she was sent away. She was fairly good at school, a good mixer, and liked company. Her brother committed incest with her often when she was aged eleven years, but when her menarche occurred at the age of fourteen years, she was not prepared for it, and was afraid of the bleeding; she did not tell her mother because she thought that what her brother had done to her had injured her, and she felt extremely guilty. She became a dressmaker until her marriage at the age of eighteen years. She had married early in the search for personal affection, but the husband had proved to be a weak reed; he was devoted to the company of men, and neither petted her nor was even good company. At times he did not speak for days; he did not help with the children, and he was apparently of a dull boorish type. The patient's condition was one of anxiety hysteria, and she was described as having cardiac neuroses. Her physical health was satisfactory, but she had had nephritis during the latter portions of her last two pregnancies; her blood pressure was slightly raised, and she had undergone thyreoidectomy seven years previously. The comment was made that the term anxiety hysteria designated those cases in which anxiety was found together with some conversion symptoms. By means of repression and displacement of symptoms from the original trouble to an external and avoidable object, some relief was obtained from the emotions set up by the trouble. In the present case the heart was selected as the substitute object. The patient had repressed the emotions attachable to her early seduction by her brother, which had later earned her a very severe beating at the hands of her father. She replaced those by dyspnœa, palpitation and pain in the chest, and by feelings of weakness and fatigue. The anxiety would be engendered by the enforced sexual abstinence, by the lack of affection she had felt all her life, and by the fear of pregnancy which the very occasional acts of coitus produced, as she was left to guard herself. The outlook for full cure was not very good, because the roots of the illness were deep-sunk and had been present for many years. Electroconvulsive therapy did not make much difference to her, and sedation and psychotherapeutic talks were being given her. It was proposed to give oxygen-carbon dioxide therapy when she could be persuaded to have that. She had had several examinations under "Sodium Pentothal" narcosis. She had had a poorly integrated personality, and her early unsatisfactory experiences as a child had given her timidity, inferiority and a lack of confidence. There had been always a desire to do things for others, as she felt that she was too inferior for them to aid her in any way, and she had never been able to take her own part in life. She had just had a course of subcoma insulin therapy.

The next patient, a single woman and invalid pensioner, aged thirty-nine years, had been admitted to the clinic in April, 1950, being referred for hysteria and certain phobias. Since an operation on her thyreoid gland seventeen years before, she had been afraid to go into trams, trains or any closed space, and had not been keen, rather strangely, on going out of her house. A little later the patient and her sister had left their parents' home, and the sister kept her while she lay in the flat or slept on a beach; this she liked doing because her fiance visited her there, and intercourse took place, of which she approved. After three years the man threw her up as being an impossibility as a future wife. In 1949 she had a second operation on her thyreoid gland, after which she had hysterical aphonia, and was unable to use her legs unless she placed the heels on the ground first, which caused a considerable degree of ataxy. She was sorry for herself, and said she feared life, and she avoided contact with others, as much as possible. She showed some retardation and wept freely. She had a course of electroconvulsive therapy and short talks of psychotherapy, and went home in three months' time. Her only physical disability in the attack was malnutrition. A year after her first admission to the clinic she began to avoid people, and to be very upset by her father whom she feared, by her mother whom she loved, and by her sister who worked and looked after her. She was afraid to travel in a public conveyance, but felt secure in a taxi; she was unable to enter a cinema or other large building. Contact with visitors left her weary and played out. She had

periods of amnesia and forgot what she had said. She forgot those things of which she did not approve. She cried easily and had attacks of palpitation, shallow breathing and tightness in the chest. She attended one concert in the amusement hall, but had to leave in a panic very soon. Her gait at times was rather insecure, and she was afraid of falling on stairs. She had been home once since admission, going to the parents' place, and she had returned in a very excited condition. She was able to help in ward work, but she could not knit or read much, because her concentration was not very good. While living with her sister in the flat, she managed to attract an odd male friend or so, when intercourse would occur, but often she had amnesia for such matters. She was regarded as having anxiety hysteria, with signs of both anxiety and conversion hysteria, and she had developed some phobias. She presented an inadequate personality, with considerable dependence on others and a keen regard for herself. Her parents had kept a strict home under the domination of a rigid male who would grant his son and two daughters no relaxation at all. There were many battles over those restrictions, and although intimidated by the father, the children were played up to by the mother, who was very easy going. They did as they liked when adolescent; the son married early for escape, and the two daughters left home to live in a flat by themselves. The girls were thus deprived of any real father influence in their early lives—that was often a feature of the ætiology in hysterics—and the death of the father early had a similar effect. The girl had been a stenographer, her fiance being her employer. After all the years of mental illness, it was not likely that a useful cure could result; such patients often deteriorated and had regressive features. Electroconvulsive therapy had not done much good. General measures, psychotherapeutic talks and physiotherapy would be persisted with. She was disinclined to have the more dynamic treatments; efforts were being made to give her a course of oxygen and carbon dioxide therapy, but she had resisted. It was explained that the thyreoidectomy and the breaking of her engagement would be important precipitating factors of her illness after the more or less traumatic childhood she had had to endure. The comment was made on phobias that anxiety could become separated from some particular worry of daily life, and the psychic energy could be placed on to some symbolic thing or situation as a definite neurotic fear. That was brought about by an unconscious mental mechanism. The results were phobias, and included fear of dirt, closed spaces, high places, contact with others and so on. The patient under discussion had shown fear of closed spaces associated with gatherings of other persons, and that no doubt had arisen from the enforced state of staying at home and in the house during her younger days at a time when her associates were out enjoying themselves. She had feared contact with her father, against whom she later rebelled.

Another patient, a married woman, aged forty-one years, had been admitted to the clinic because of collapse with amnesia and retention of urine. She worked as a secretary in a city office, and had been looking after her sick mother after work. That entailed much night work, as the mother had a cardio-renal condition, and needed a lot of attention. The mother had recently died, and the patient collapsed after her long period of double duty. She could not see, felt giddy, had dry vomiting, and felt very weak. She was afraid of everything, and felt that she should have done more for her mother. She could not sleep, was unable to concentrate and had considerable amnesia; with strangers her mind went blank, and she conducted a poor conversation. She was agitated, depressed and irritable, and anxious lest she become like her mother. Investigation revealed that her home life had been happy; her education was fair, and her tastes had run to exhibition dancing. She was under the sway of her father, who was aged seventy-six years. Her marriage at the age of twenty years was a failure; she had chosen her dancing partner, who turned out to be a worthless rogue, and she divorced him. For some time before coming to the clinic she had been having sex relations with a married man (*coitus interruptus*) and that gave her a sense of frustration and guilt; she made matters worse by avoiding orgasm. She feared lest she hurt her father, who demanded all her attention, but gave his time and affection to a young niece who lived in the home. She was torn between conflict of duty to her father, and her wish to be *de facto* wife to another man and move from home. The strain of that, and sex frustrations, had set up the present illness. The storm burst when the mother died and no longer needed her in the home, making it possible for her to leave the father. Between two strong conflicting wishes she had fallen, and sought safety in illness. It was considered that electroconvulsive therapy and explanatory talks would result in her cure. The comment was made that an anxiety state was the first form of many types of psychological disorder, but it was not as a rule very rapid in onset, as contrasted, for example, with hysteria. A person might notice that he was not able to do things he could do formerly with ease, or that worries were getting a grip of him unknown before. Lack of sleep, and of appetite, rapid pulse, perspiration and anxiety were the early symptoms; then conversion symptoms often appeared in the form of dyspnœa, pain in the chest, amnesia, loss of bladder function and so on, and there resulted the disorder known as anxiety hysteria. Often the anxiety symptoms themselves became hysteroid in character, partly because medical men did not always follow the psychological matters. The patient might then complain of palpitation, vertigo and nausea, but might state that he was free of anxiety, in other words, feelings of apprehension and depression. Those extensions to the hysterias would occur often late in the history of the illness. The patient shown had had a course of electroconvulsive therapy with some mental gains and considerable bodily improvement. She had just completed a course of some 30 subcoma insulin treatments and had benefited a great deal in all ways.

The last patient in the group, a married man, aged thirty-five years, with one child, was a storeman and a native of Yugoslavia. He had been admitted to the clinic recently because he suffered from pains without any demonstrable organic basis. His appendix had been removed in Germany in 1948. In January, 1950, he had had an operation for adhesions, but none were found. He then said that he had headaches, blurred vision, ringing in the ears, and pain in the appendix area. Mentally he could not concentrate and was anxious and irritable. He said that he might die, or remain incurable, and that was the reason why he could not bring his wife and child to Australia (they were still in Germany). He said that nobody wanted to get him well, and he felt depressed and so miserable that he could take his life; he believed his strength was oozing away from him by means of the perspiration with which the palms of his hands were covered. The head pains were chiefly on the right side of his head, and sunshine was the agent that freed them. He felt well from 6 p.m. to 9 a.m. The background was that he came of a good family in Belgrade, and had been a bank clerk until war broke out; from then until 1945 he was a prisoner of war in Germany, and had many hardships. He married a German girl in 1947, and had a child. They would be brought to Australia as soon as he signed a certain form, but his eyes blurred and his hand trembled too much when he went to sign the paper. His condition was considered to be acute anxiety hysteria. The comment was made that many New Australians suffered in a similar way. The patient blamed lack of sex life for his trouble, and he was probably to some extent correct. He had no money, spoke English badly, and had to take a job as storeman, for which he was not suited by desire or strength. His illness must represent his inability to work in a menial occupation; his worry over his wife, child, money and future was seen in the anxiety. That was conscious, and had been explained to him, but the hysteria part of his illness, as seen in the conversion symptoms, was an escape from the unconscious, and caused him more serious disability. He would make a satisfactory recovery, and that would be hastened by the arrival of his wife and child. Short talks of a psychotherapeutic nature were the best form of treatment, to be used with sedation as indicated. Electroconvulsive therapy had calmed his early agitation, and rendered him able to talk reasonably about his condition. He had had a course of subcoma insulin therapy and was very much better in his mental outlook.

Huntington's Chorea.

Two patients were shown who were suffering from Huntington's chorea. It was explained that amongst the degenerative nervous diseases which manifested themselves in middle life, one of the most striking was chronic progressive chorea. It was usual in Australia to see the hereditary form described by Huntington, but progressive degeneration with choreic manifestations occurred in which the hereditary element was lacking. The characteristics of Huntington's chorea were progressive mental deterioration, choreiform movements and the hereditary transmission of the condition as a Mendelian dominant. Symptoms usually manifested themselves in the fourth or fifth decade, but they might not appear until late in life. Occasionally, on the other hand, they showed up in the first and second decades, an example of the phenomenon of anticipation. Since the hereditary factor was a Mendelian dominant, 50% of the children of a choreic subject could be expected to inherit the disease; that was assuming, of course, that the choreic

subject was a hybrid, the result of the mating of a choreic and a non-choreic subject. A pure-bred choreic subject would have 100% of choreic children. All the possibilities mentioned did occur occasionally in isolated communities. In the family of a patient who had recently been under treatment at the clinic, the father was one of eleven siblings, five of whom were choreic. The first of the patients to be presented had chorea, and her sister also had it. They had two non-choreic siblings. The classical symptoms were chorea and mental decay with appearance in adult life and a progressive course. Each character of the condition was subject to modification. For example, there might be chorea without dementia or the reverse, and the onset might be in early or in late life; the course might be slow or rapid.

The first patient presented was a married woman, aged forty-two years, who had one child. She had been admitted to the clinic in December, 1949, because she had depression associated with progressive chorea and mental deterioration. Her mother, her maternal grandmother and two maternal uncles had all suffered from Huntington's chorea. The patient's illness had started about two and a half years previously, when she had become irritable and hard to get on with. She worried constantly and was continually nagging. She could not walk straight, and was clumsy with her hands. The chorea consisted of movements of the limbs and trunk which were continuously present; they occurred at any time, especially when she was doing things. Mentally her attention was poor, she could not concentrate well and her affect was rather labile. She gave a poor repetitive story of her illness, she giggled strangely and her voice altered at times. She complained of a blank feeling in her head and of severe headaches. She was very talkative. At the time of the meeting she was not yet fully demented, but she had progressed considerably in that direction during the past year. She went out for two days' leave at the week-end and was still able to preserve some of her former social poise. The prognosis was that the condition might go on for ten or twenty years. It was pointed out that the pathological conditions involved the whole brain; but the essential lesions, consisting of atrophy of cells and fibres, were predominantly in the cortex and basal ganglia. Miliary encephalitic foci with secondary atrophy were found scattered throughout the brain. Ganglion cells of the cortex degenerated and were replaced by glial cells and fibres. The *corpus striatum* was shrunken in places, and the smaller cells especially were degenerated. Treatment was supportive and sedative only.

The second patient with Huntington's chorea was a married man, aged forty-seven years. He had one child and was a salesman by profession. He had been admitted to the clinic on July 24, 1950, because of progressive chorea associated with mental instability. The choreic movements had progressed to the present severe and disabling proportions steadily over a period of two and a half years. He had pains in the head which prevented him from going to work at intervals; but it was not until three months before his admission to the clinic that he had begun to act strangely. He began to make bogus claims; for example, he said that he had twice received considerable bonus cheques from his employers, although that was quite untrue. The facts were that he could not concentrate, had become strange in manner and rather effusive and euphoric, and had been paid off finally because of irresponsibility. He had also said that the grocer's shop belonged to him, and that he had ordered a motor-car for his own use in the business. He was lacking in insight into his false beliefs, and still claimed to be in receipt of £300 a week and to have just bought a new house. The patient's father had been a mental patient, and had died three years after the onset of choreic movements in the head and limbs. The patient's brother was "nervy", but his sister was free of trouble so far. The patient had had a college education, but had taken positions beneath his proper status, and had preferred being a shop salesman to more lucrative positions. He was a teetotaller, but a heavy smoker. He was in fair general health, with no ailments apart from the cerebral disease. His reflexes were all increased, excepting the abdominal reflexes, which were normal. The results of serological examination of both his blood and his cerebro-spinal fluid were negative. The comment was made that the familial nature of the disease was well enough established from the father's illness, but as well there was a non-familial form of chronic progressive chorea with dementia. The illness became manifest in the third and fourth decades as a rule, and as a result many of the sufferers had sons and daughters of whom 50% would probably develop the complaint. To prevent the continuance of the disease it would be necessary to sterilize those persons having known hereditary tendencies before they were of an age to breed. That procedure was not likely to be accepted in a community in which sterilization of known mental defectives was not tolerated. There was no cure for the disease, and all that was needed was care and attention with treatment of symptoms as they arose.

Paraphrenia.

A group of patients was presented suffering from paraphrenia of the amorous and the persecutory types. The first, a single woman, aged forty-three years, a domestic servant, had been admitted to the clinic on October 4, 1950, because she felt that people were passing through her to each other and she feared injury at their hands. Since the death of her mother eighteen years earlier she had been at loggerheads with the family members because of her fancies. She dreamed the fancies, but as dreams she claimed that they were real. She used to hear voices, and put that down to mental telepathy. She was afraid to go to sleep because she had sexual dreams, and on waking she felt sure that sexual intercourse had taken place. She felt an after-image of external pressure against her body,

(To be continued.)

Correspondence.

GESTATIONAL RUBELLA AND THERAPEUTIC ABORTION.

SIR: In two discussions reported in your columns (September 9, 1950, pages 389-394 and page 418; November 25, 1950, pages 806-810) epidemiologists, pædiatricians and obstetricians have given their views on this subject. Let me now crave the immemorial right of the amateur to analyse scientifically the material which the specialists provide.

Professor Mayes (page 808) gives views which, he says, are personal and not scientific; he advocates abortion in order that the mother may be spared from worry. Before agreeing with this opinion we are entitled to a scientific survey proving that the embryo is affected in a large proportion of cases of rubella. But such scientific evidence is non-existent; Anderson (page 389) quotes only 44 cases from the literature, and all the speakers agree that the collection of reliable statistics is a matter of prime urgency. But how can we obtain scientific data if by indiscriminate abortions we are destroying the necessary material? Perhaps a large-scale survey of rubella in pregnancy would show that the proportion of grossly handicapped children is smaller than the 1:10 which Lemmon (page 392) sets as a possible lower limit. McLorinan (page 390) reports three cases which went to term; all the children were normal.

Furthermore, we lack reliable diagnostic criteria for rubella. McLorinan, whose clinical knowledge is second to none, enumerates four factors which make diagnosis difficult; he says further: "I, for one, would welcome some laboratory diagnostic aid, realizing that the decision may sometimes be fraught with tremendous consequences. . . . I wonder in how many of these cases the diagnosis may have been infective mononucleosis with a morbilliform rash. The differential diagnosis, apart from measles and scarlet fever, includes a host of conditions which cause a rash." Colebatch (page 418) often cannot be certain whether the patient had rubella or *exanthem subitum*.

Let us now suppose that 100 abortions have been performed on successive patients. That the diagnosis should be correct in 80 is as much as we can expect; that is, 20 normal children have been destroyed through pardonable errors in diagnosis. Of the 80 correctly diagnosed, Lemmon suggests that the number of children who would have been grossly handicapped is not more than 20 nor less than eight. Therefore 100 abortions would have destroyed not more than 92 nor less than 80 reasonably healthy children. And what proportionate benefit is promised by those who advocate such unscientific slaughter? None whatever, except the elimination of a small number of congenital defects whose study, everyone admits, is one of the most promising fields of medical research today.

In order to save women from worry, it appears, scientists are advocating a procedure that will not only slaughter a very large number of healthy children, but will destroy all evidence that can tell how serious are the grounds for worry, and at the same time close a fruitful avenue of research.

Let us now examine from another angle the reality of the grounds for worry. Lemmon says that there is no obstetrical problem, but only a psychiatric one; he says further that there is great divergence of opinion among psychiatrists on the desirability of abortion. Thus the death or survival of a child may well depend upon which psychiatrist one happens to consult. It is common knowledge that many practitioners today are "creeping under the umbrella so invitingly held out by the psychiatrist" (Lemmon).

There is more than one way in which the patient can be protected from anxiety: (i) If rubella is suspected, do not tell her. The doctor who is worthy of the name should be anxious to shield his patient. If he feels it necessary to protect himself, he may inform another member of the family, but the young mother should be shielded from anxiety. Every doctor has to bear burdens like these every day, and if he does not accept them he should not have been a doctor. (ii) If the patient knows that rubella is suspected, she should be told all the truth, which is that the odds are at least five to one in favour of a reasonably healthy child. And surely this should quiet her anxiety. What expectant mothers do not undergo tormenting fears of deformity in their babies? The doctor should strengthen and encourage his patient rather than surrender to her weaker moods.

Those who advocate abortion do so on emotional grounds only; they are mistakenly kind-hearted, as Professor Mayes admits; his opinion is personal and decidedly not scientific. Yet Professor Dods (page 806) caricatures the forces which would preserve life as "a frightening aura of religious, moral, emotional and legal considerations" opposed to his "realistic consideration of the evidence". Professor Mayes, while not claiming to be scientific, yet manages to turn the issue into a straight conflict between science and religion.

There is no such conflict; science is on the side of the angels.

Yours, etc.,

M. KELLY.

"Stanhill",
34 Queens Road,
Melbourne.
December 6, 1950.

AUSTRALIAN RED CROSS APPEAL FOR DRUG SAMPLES.

SIR: Following the publication in your journal of the need for drugs in Indonesia and our appeal to medical practitioners to send in samples, we have had an excellent response, but, of course, the need is very great.

Included in a parcel received were two service stars, the 1939-1945 and Pacific. Unfortunately there is no indication on or in the parcel of the identity of the sender, and we were wondering if you would be good enough to include in a future issue of your journal a note to the effect that these service stars have been found and are being held at this headquarters.

Yours, etc.,

A. B. CHALLICE,
General Secretary.

Australian Red Cross Society (New South Wales Division),
27 Jamieson Street,
Sydney.
December 12, 1950.

CARE AND MANAGEMENT OF LABORATORY ANIMALS.

SIR: In 1943 we were seeking information about the care and management of laboratory animals and were able, through the hospitality of your columns, to make contact with many scientists using laboratory animals. Thanks to this help and to that of certain expert writers we were able to issue in 1947 the "UFAW Handbook on the Care and Management of Laboratory Animals", edited by Professor A. N. Worden, M.R.C.V.S. As some time has now elapsed since this book appeared, we should be most grateful if we might again appeal to all persons interested in laboratory animals to send us suggestions for the improvement of the handbook and any additional information which has come to their notice. The subjects concerning which information is required are as follows: the training of animal technicians, animal houses and animal rooms, rabbits, guinea-pigs, rats, mice, voles, hamsters, hedgehogs, ferrets, frogs and other amphibians, fish, anthropoids, dogs, cats, goats, poultry, canaries, pigeons, or any other species of animals used for scientific purposes.

Subject matter can be conveniently forwarded to us grouped under the headings of anæsthesia, euthanasia, supply and breeding, feeding and watering, general management and hygiene, transport by sea, land and air, animal behaviour and psychology.

All the information which reaches us will be most gratefully acknowledged.

Yours, etc.,

F. JEAN VINTER,
Technical Secretary, The Universities Federation for Animal Welfare.

284 Regent's Park Road,
Finchley,
London, N.3.
November, 1950.

CONGENITAL DEAF-MUTISM, PIGMENTARY DEGENERATION OF THE RETINA, AND AMENTIA.

SIR: My article, "Congenital Deaf-Mutism, Pigmentary Degeneration of the Retina, and Amentia", published recently in THE MEDICAL JOURNAL OF AUSTRALIA, resulted in a communication from Mr. W. E. Johnson, Superintendent of the New South Wales Institution for the Deaf and Dumb and the Blind, at Darlington. This communication contains some pleasing (and corrective) information, which I feel obliged to make known.

With regard to his institution he states: "Children are admitted at any time after reaching the age of four years, and in two instances last year, children of three years eight months and three years ten months were accepted. There is a section of the school that is organised on nursery school lines, and has been in existence for almost four years. At present there is a scheme in hand for parent and child pre-school education, and I hope to have it organised early in the New Year." It is good to know that the situation with regard to the pre-school training of deaf children is not as black as I painted it.

He corrects me on a further point (on which I had previously been misinformed), stating that his School for the Deaf at the Darlington Institution has not been taken over by the Department of Public Instruction. It is still a private school maintained by voluntary contributions.

Yours, etc.,

B. H. PETERSON.

Mental Hospital,
Parramatta,
New South Wales.
December 20, 1950.

TREATMENT OF ECZEMA.

SIR: My heart used to sink if I ever saw a mother bring a baby with eczema into the surgery. Treatment seemed to make so little difference. And adults with generalized eczema were not much better. However, three years ago I heard of a mixture, devised by a Melbourne chemist, for infantile eczema; and the way patients began to come to the surgery, even from long distances, when they heard that my partners and I were using the prescription, seemed rather a good advertisement for its efficacy. Speaking from memory, we had treated 30 cases by the time I left Melbourne, with 28 very satisfactory results. Even the two comparative failures did better than the cases I had seen treated by orthodox methods—admittedly not very many; the general practitioner does not usually see a great number of infantile eczemas. The medicine does not bring about a permanent cure. Relapses are common; but all one has to do is to prescribe another course, which mothers accept gratefully. The same chemist also has a treatment for adult eczema, which also gave very good results; and two patients with psoriasis were quite definite that it cured them—again, temporarily.

It seems rather silly to write about a medicine, when one has not had much opportunity for about two years of using it. But it seems equally silly not to make such a satisfactory treatment as widely known as possible. Here are the chemist's directions, and the prescriptions. They are rather polypharmaceutical, but I have never been game to drop any of the ingredients.

For infants over six months:

℞

Sodii citratis	20 grains
Sodii bicarbonatis	10 grains
Liquoris arsenicalis	1 drachm
Lactis bismuthi	3 drachms
Lactis magnesii	6 drachms
Syrupi simplicis	3 drachms
Aquam anisi ad	4 fluid ounces

Signature.—One drachm three times a day after meals till skin is perfect; then twice a day for ten days more.

For adults:

"A"

℞

Sodii bicarbonatis	4 drachms
Potassii bicarbonatis	3 drachms
Liquoris ammoniæ diluti	1·5 drachms
Liquoris arsenicalis	1 drachm
Tincturæ rhei compositæ	2 fluid ounces
Spiriti chloroformi	70 minims
Extracti glycyrrhizæ liquidi	2·5 drachms
Aquam menthæ piperitæ ad	10 fluid ounces

"B"

℞

Bismuthi oxycarbonatis levis	2 drachms
Liquoris arsenicalis	1 drachm
Misturam "A" ad	10 fluid ounces

Signature.—One-half fluid ounce three times a day after meals; take "A" and "B" on alternate days.

There has been a case of death from arsenical poisoning in a patient taking this medicine. But apparently he had decided, off his own bat, to take a double dose; and continued to do so, regardless of symptoms. The dose as prescribed is well within the British Pharmacopœia range.

Senior members of the profession are apt to remark loftily: "Oh, yes, of course, arsenic *is* good." Then why on earth don't they use it, and give parents of eczematous babies a bit of sleep at night?

Yours, etc.,

D. A. BRITTEN.

13 Clive Road,
Mount Lawley,
Western Australia.
December 21, 1950.

OCULAR MANIFESTATIONS OF SARCOIDOSIS WITH A DESCRIPTION OF SEVEN CASES.

SIR: In reply to Miss Lewis I would state that sarcoidosis was first described by Jonathan Hutchinson in 1869, and no one has ever found a cause.

In 1946 Ferrié and Grynfelt reported three cases of ocular sarcoidosis proved by biopsy. In the first case the Mantoux test provoked focal reactions in eye and arm. In the second the Mantoux reaction was strongly positive. In the third case guinea-pig inoculation gave positive results. They conclude that the disease is an atypical tuberculosis.

Until a causal organism is found, surely it is wise to call these cases tuberculous manifestations.

Yours, etc.,

F. W. SIMPSON, D.O. (Oxon.).

105 Saint George's Terrace,
Perth,
December 20, 1950.

POST-GRADUATE HOSPITAL POSTS IN ENGLAND.

SIR: As this hospital residency year is coming to a close, the Post-Graduate Committee in Medicine in the University of Sydney has been approached by increasing numbers of recent graduates wishing to proceed overseas.

The committee desires to point out that the resident hospital position in England has altered materially in the past eighteen months. All the teaching hospitals and many of the larger non-teaching hospitals are used as pre-registration hospitals for new graduates, and it is therefore unlikely that many overseas graduates would be able to gain a post in hospitals of this kind. Registrar posts are likewise more difficult to obtain as the number available at all hospitals has been drastically reduced. For such positions, local graduates would naturally have priority.

The Post-Graduate Committee feels that it is unwise for recent graduates with early experience only to proceed overseas until they are more medically mature and have completed at least two years of their basic practical training.

Yours, etc.,

A. M. MCINTOSH,
Chairman, The Post-Graduate Committee in Medicine in the University of Sydney.

131 Macquarie Street,
Sydney,
December 22, 1950.

OCCUPATIONAL OPHTHALMOLOGY.

SIR: In the review recently of Mr. Joseph Minton's "Occupational Eye Diseases and Injuries", I would like to draw attention to some of the reviewer's remarks concerning removal of corneal foreign bodies. As one who has had a large experience of corneal foreign bodies including house positions at two eye hospitals, one in conjunction with Mr. J. Minton, I would like to point out that experience of covering with a pad and bandage, after removal, till next morning, has offered best results and most comfort to the patient. Does the reviewer send the patient out without any covering at all and leave the anæsthetized cornea open to the possibility of another foreign body?

I agree with the reviewer concerning the ring of rust with ferrous foreign bodies, but cannot agree that a Bowman's needle should not be in the armamentarium of the corneal foreign body remover. With a dental burr, the needle can be used for practically all corneal foreign bodies. Does the reviewer wish to revert to the eye spud? Is the reviewer really serious when he says that the patient should resume work immediately? I would suggest that the reviewer have a foreign body, where removal has caused penetration of the Bowman's membrane, and then continue his work as an ophthalmologist at once.

Yours, etc.,

S. R. GERSTMAN.

32 Collins Street,
Melbourne,
November 24, 1950.

[The reviewer of Minton's book, who has had many years of practical experience in industrial ophthalmology, was, with some delay and difficulty, sent a copy of Dr. Gerstman's letter. He replies that for twenty-five years he has used no bandage for eyes from which corneal foreign bodies have been removed. When a wounded cornea is not covered by the lids it is virtually painless. The only way to eliminate real discomfort is to bandage both eyes. The reviewer states that he does send the anæsthetic cornea into "the wide open spaces" and that he has never had any untoward result from doing so, even before he discarded the use of cocaine as an anæsthetic. He draws attention to the rapid epithelial regeneration which occurs under the best conditions (those used by him). The reviewer does not withdraw his condemnation of Bowman's needle for the removal of foreign bodies and he wonders why, if the needle is so good, a burr has to be added to the tool kit. He has discarded the use of the burr as it causes too much trauma. The spud is in his opinion a deadly weapon with an effect something like that following the use of a plough in a herbaceous border. He makes his own instruments for the removal of foreign bodies and has three different sizes, used according to the area of the lesion. They are made from old Graefe knives and needles of the knife type, the only unsuitable one being Bowman's. The reviewer is serious when he suggests that the patient should resume work at once; suitable treatment is given when necessary as well as advice to resume work. He has seen injuries of the type mentioned in Dr. Gerstman's last sentence caused in workshops and has carried out his own type of treatment.—EDITOR.]

Obituary.

THOMAS RHODES MATSON.

WE regret to announce the death of Dr. Thomas Rhodes Matson, which occurred on December 21, 1950, at Melbourne.

RUPERT GORDON WEAVER.

WE regret to announce the death of Dr. Rupert Gordon Weaver, which occurred on January 3, 1951, at Melbourne.

CLIVE NELSON PITT.

WE regret to announce the death of Dr. Clive Nelson Pitt, which occurred on January 3, 1951, at London, England.

GEORGE WADE SINCLAIR.

WE regret to announce the death of Dr. George Wade Sinclair, which occurred on January 7, 1951, at Eastwood, Sydney.

GEORGE EDWARD MURPHY.

WE regret to announce the death of Dr. George Edward Murphy, which occurred on January 7, 1951, at Armadale, Victoria.

Medical Practice.

POLICE OFFENCES (AMENDMENT) ACT, 1908, AS AMENDED.

THE following proclamation, relating to certain drugs which are analogues of "Amidone" and of pethidine, is published in the *New South Wales Government Gazette*, Number 190, of December 15, 1950.

I. Sir John Northcott, Knight Commander of the Most Distinguished Order of Saint Michael and Saint George, Companion of the Most Honourable Order of the Bath, Member of the Royal Victorian Order, Lieutenant-General on the Retired List of the Australian Military Forces, Governor of the State of New South Wales and its Dependencies in the Commonwealth of Australia, with the advice of the Executive Council, do, by this my Proclamation, declare that Part VI of the *Police Offences (Amendment) Act*, 1908, as amended, shall apply to:

Alphaprodine (α-4-propionoxy-4-phenyl-1: 3-dimethyl-4-piperidine), its salts and any preparation, admixture, extract or other substance containing any proportion of alphaprodine.

Betaprodine (β-4-propionoxy-4-phenyl-1: 3-dimethyl-4-piperidine), its salts and any preparation, admixture, extract or other substance containing any proportion of betaprodine.

Hydroxypethidine (ethyl 4-η-hydroxyphenyl-1-methyl-piperidine-4-carboxylate), its salts and any preparation, admixture, extract or other substance containing any proportion of hydroxypethidine.

Isoamidone (6-dimethylamino-4: 4-diphenyl-5-methyl-hexan-3-one), its salts and any preparation, admixture, extract or other substance containing any proportion of isoamidone.

Ketobemidone (4-propionyl-4-η-hydroxyphenyl-1-methyl-piperidine), its salts and any preparation, admixture, extract or other substance containing any proportion of ketobemidone.

Methadol (6-dimethylamino-4: 4-diphenylhepatan-3-ol), its salts and any preparation, admixture, extract or other substance containing any proportion of methadol.

Methadyl acetate (6-dimethylamino-4: 4-diphenyl-3-heptyl acetate), its salts and any preparation, admixture, extract or other substance containing any proportion of methadyl acetate.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED DECEMBER 23, 1950.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.[2]	Northern Territory.[2]	Australian Capital Territory.[2]	Australia.[2]
Ankylostomiasis	*	..	..	..	..	..	..	..	..
Anthrax	*	..	..	..	..	..	..	..	..
Beriberi	*	*	*	*	*	*	..	*	..
Bilharziasis	*	..	..	..	..	..	..	..	..
Cerebro-spinal Meningitis	2(1)	1	..	..	..	..	..	..	3
Cholera	..	..	..	..	..	..	..	..	..
Coastal Fever(*a*)	*	*	*	*	*	*	*	*	..
Dengue	*	*	*	*	*	*	..	*	..
Diarrhœa (Infantile)	..	..	7(7)	..	..	..	..	..	7
Diphtheria	6(4)	3(2)	2(2)	..	4(2)	..	..	..	15
Dysentery (Amœbic)	*	..	..	..	..	..	..	..	..
Dysentery (Bacillary)	*	2(2)	1(1)	..	3(3)	..	..	..	6
Encephalitis Lethargica	..	..	..	..	..	..	..	..	..
Erysipelas	*	*	*	1	*	*	..	..	1
Filariasis	*	..	..	..	..	..	..	..	..
Helminthiasis	*	..	*	*	*	*	*	*	..
Hydatid	*	..	*	*	..	*	*	..	..
Influenza	*	*	*	..	*	*	..	*	..
Lead Poisoning	*	*	..	*	*	*	*	*	..
Leprosy	..	..	..	..	..	..	..	..	..
Malaria(*b*)	*	..	2(1)	..	..	..	..	..	2
Measles	*	*	*	212(42)	*	*	..	..	212
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	42(22)	3(1)	12(4)	14(12)	1(1)	..	..	..	72
Psittacosis	*	..	*	..	*	*	*	*	..
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella(*c*)	*	*	..	*	..	*	..	..	..
Scarlet Fever	19(6)	16(3)	10(6)	4(3)	6(5)	..	..	..	55
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	*	..	1	*	*	*	*	*	1
Trachoma	*	..	*	*	*	*	*	*	..
Tuberculosis(*d*)	14(9)	10(7)	3(3)	9(8)	14(6)	..	..	..	50
Typhoid Fever(*e*)	..	..	..	1(1)	1	..	..	..	2
Typhus (Endemic)(*f*)	..	..	..	..	..	..	..	..	..
Undulant Fever	..	..	..	..	..	..	..	..	..
Weil's Disease(*g*)	*	*	*	*	*	*	*	*	..
Whooping Cough	*	*	*	4(2)	*	*	..	..	4
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] The form of this table is taken from the *Official Year Book of the Commonwealth of Australia*, Number 37, 1946–1947. Figures in parentheses are those for the metropolitan area.
[2] Figures not available.
[3] Figures incomplete owing to absence of returns from the Northern Territory, Australian Capital Territory and Tasmania.
* Not notifiable.
(*a*) Includes Mossman and Sarina fevers. (*b*) Mainly relapses among servicemen infected overseas. (*c*) Notifiable disease in Queensland in females aged over fourteen years. (*d*) Includes all forms. (*e*) Includes enteric fever, paratyphoid fevers and other Salmonella infections. (*f*) Includes scrub, murine and tick typhus. (*g*) Includes leptospiroses, Weil's and para-Weil's disease.

Phenadoxone (also known as heptalgin) (6-morpholino-4: 4-diphenylheptan-3-one), its salts and any preparation, admixture, extract or other substance containing any proportion of phenadoxone;

in the same manner as it applies to the drugs mentioned in paragraph (a) of subsection 2 of section 18 of the said Act.

Signed and sealed at Sydney, this 29th day of November, one thousand nine hundred and fifty.

By His Excellency's Command,

CLIVE EVATT.

Medical Appointments.

Dr. P. M. Nicholls has been appointed honorary medical officer at the Mount Gambier Hospital, South Australia.

Dr. T. G. C. Retallick has been appointed medical superintendent of the Mental Hospital, Kew, Victoria.

Dr. H. C. Stone has been appointed medical superintendent of the Mental Hospital, Sunbury, Victoria.

Dr. J. Catarinich has been appointed Acting Director of Mental Hygiene, Victoria.

Dr. J. F. J. Cade has been appointed medical superintendent of the Repatriation Mental Hospital, Bundoora, and the Mental Hospital, Janefield, Victoria.

Dr. Stephen G. Sandes has been appointed deputy medical superintendent, Division of Mental Hygiene, Department of Public Health, New South Wales.

Dr. T. N. Rowlands has been appointed a member of the Board of Optometrical Registration of New South Wales.

Dr. G. G. Wyllie has been appointed surgical registrar at the Royal Adelaide Hospital, Adelaide.

Dr. J. Zimmet has been appointed honorary clinical assistant to the dermatological section of the Royal Adelaide Hospital, Adelaide.

Dr. W. V. Rowe has been appointed honorary clinical assistant to the ophthalmological section of the Royal Adelaide Hospital, Adelaide.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Short, Donald Wheeler, M.B., 1951 (Univ. Sydney), Temora District Hospital, Temora, New South Wales.

Tracy, Graham Douglas, M.B., 1948 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.

Shapiro, Colleen Juanita Ann, M.B., B.S., 1950 (Univ. Sydney), District Hospital, Bathurst.

Tellesson, Thomas Keith, M.B., B.S., 1951 (Univ. Sydney), Hornsby and District Hospital, Hornsby.

Tellesson, William George, M.B., B.S., 1951 (Univ. Sydney), Sydney Hospital, Macquarie Street, Sydney.

Hooper, James Hamilton, M.B., B.S., 1950 (Univ. Sydney), Parramatta Hospital, Parramatta.

Furber, James Gordon, M.B., B.S., 1951 (Univ. Sydney), 580 New South Head Road, Double Bay.

Marshall, Martin Hamilton, M.B., B.S., 1951 (Univ. Sydney), 21 Ormond Street, Ashfield.

Michell, George, M.B., B.S., 1950 (Univ. Sydney), Sydney Hospital, Macquarie Street, Sydney.

Morrison, Dorothy Mary, M.B., B.S., 1950 (Univ. Sydney), 5 Muston Street, Mosman.

Myers, Geoffrey Stratford, M.B., B.S., 1950 (Univ. Sydney), Lithgow Hospital, Lithgow.

Rail, Wilton Whitburn, M.B., B.S., 1941 (Univ. Melbourne), Sheridon Street, Gundagai, New South Wales.

Sheaves, Bruce Boyd, M.B., B.S., 1947 (Univ. Sydney), 41 Port Hacking Road, Caringbah.

Diary for the Month.

JAN. 23.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JAN. 24.—Victorian Branch, B.M.A.: Council Meeting.
JAN. 26.—Queensland Branch, B.M.A.: Council Meeting.
FEB. 1.—South Australian Branch, B.M.A.: Council Meeting.
FEB. 2.—Queensland Branch, B.M.A.: Branch Meeting.
FEB. 6.—New South Wales Branch, B.M.A.: Organization and Science Committee.
FEB. 7.—Western Australian Branch, B.M.A.: Council Meeting.
FEB. 9.—Queensland Branch, B.M.A.: Council Meeting.
FEB. 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
FEB. 20.—New South Wales Branch, B.M.A.: Medical Politics Committee.
FEB. 22.—Victorian Branch, B.M.A.: Executive Meeting.
FEB. 22.—South Australian Branch, B.M.A.: Branch Meeting.
FEB. 23.—Queensland Branch, B.M.A.: Council Meeting.
FEB. 26.—Federal Council, B.M.A. in Australia: Meeting at Melbourne.
FEB. 27.—New South Wales Branch, B.M.A.: Ethics Committee.
FEB. 28.—Victorian Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney)—All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia; Medical Officer, South Australian Railways.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

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